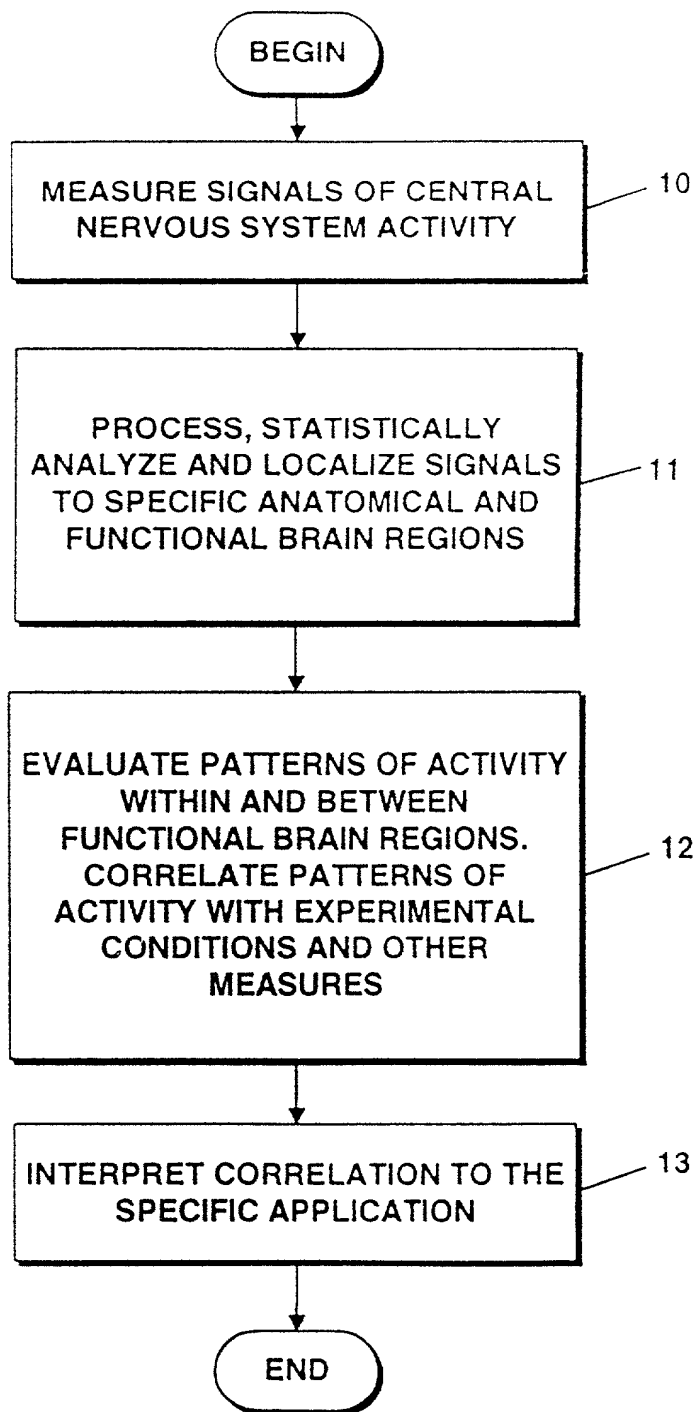METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
CASE NO. MGH-004BUS

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BEGIN
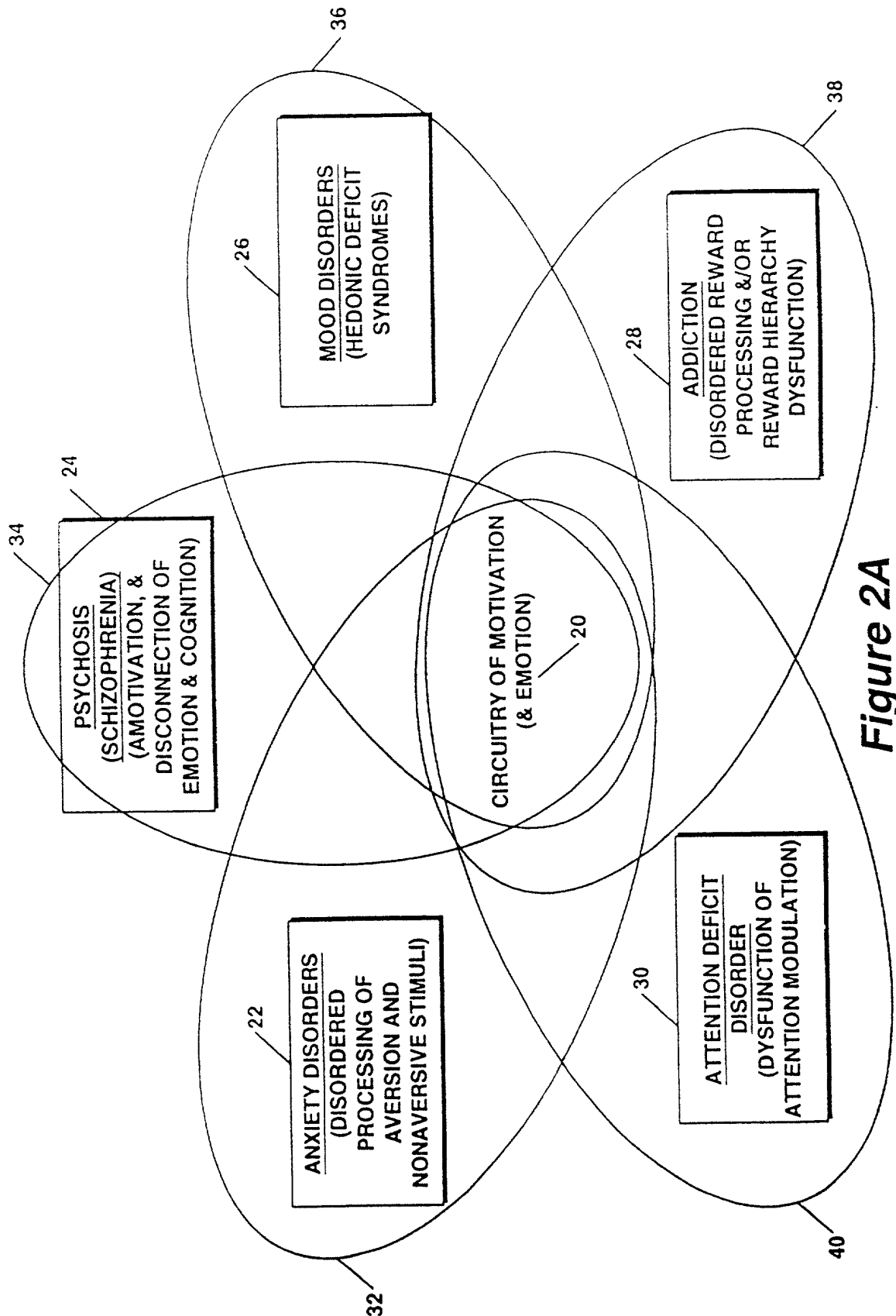
MEASURE SIGNALS OF CENTRAL NERVOUS SYSTEM ACTIVITY — 10

PROCESS, STATISTICALLY ANALYZE AND LOCALIZE SIGNALS TO SPECIFIC ANATOMICAL AND FUNCTIONAL BRAIN REGIONS — 11

EVALUATE PATTERNS OF ACTIVITY WITHIN AND BETWEEN FUNCTIONAL BRAIN REGIONS. CORRELATE PATTERNS OF ACTIVITY WITH EXPERIMENTAL CONDITIONS AND OTHER MEASURES — 12

INTERPRET CORRELATION TO THE SPECIFIC APPLICATION — 13

END

Figure 1

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
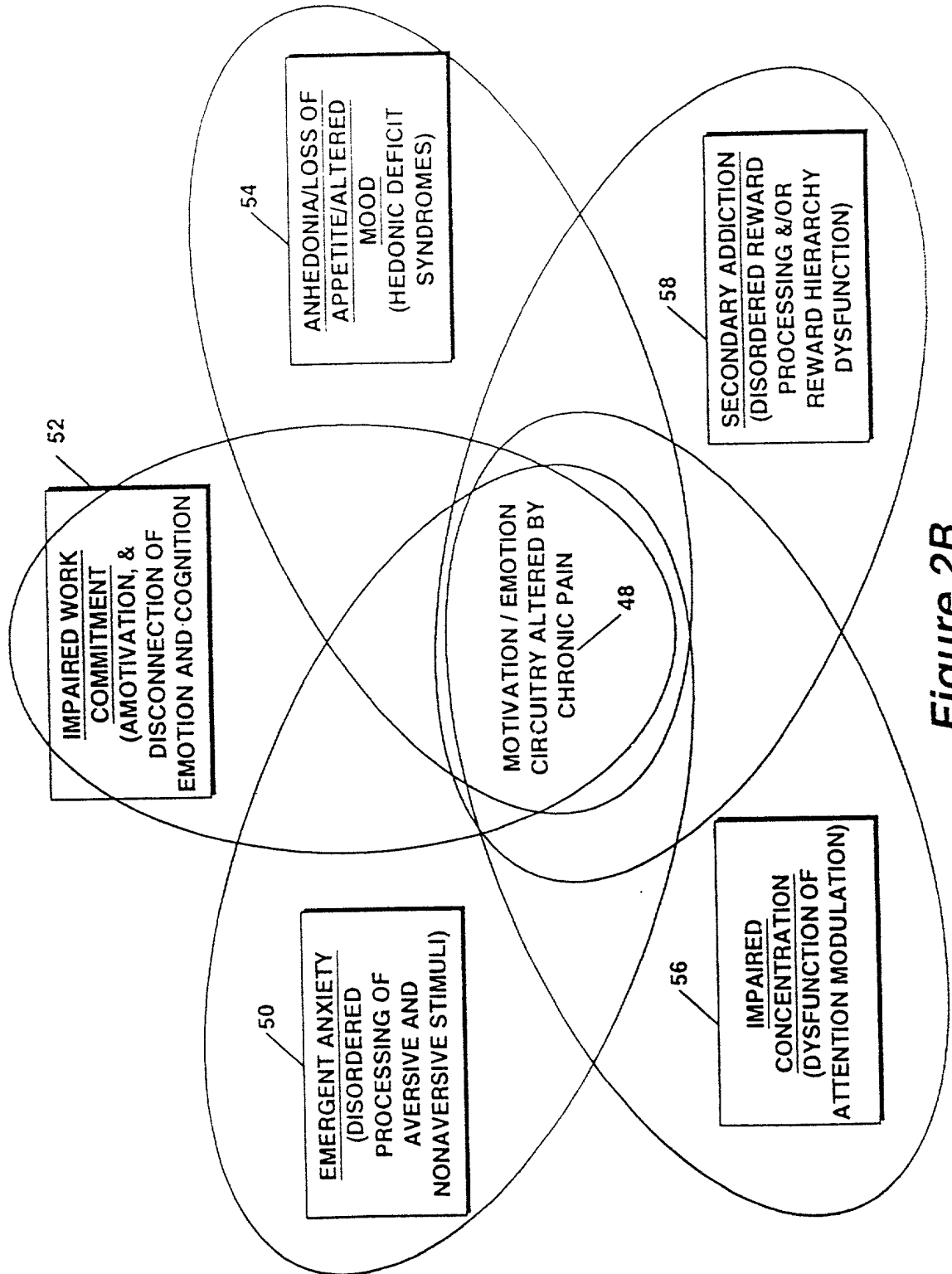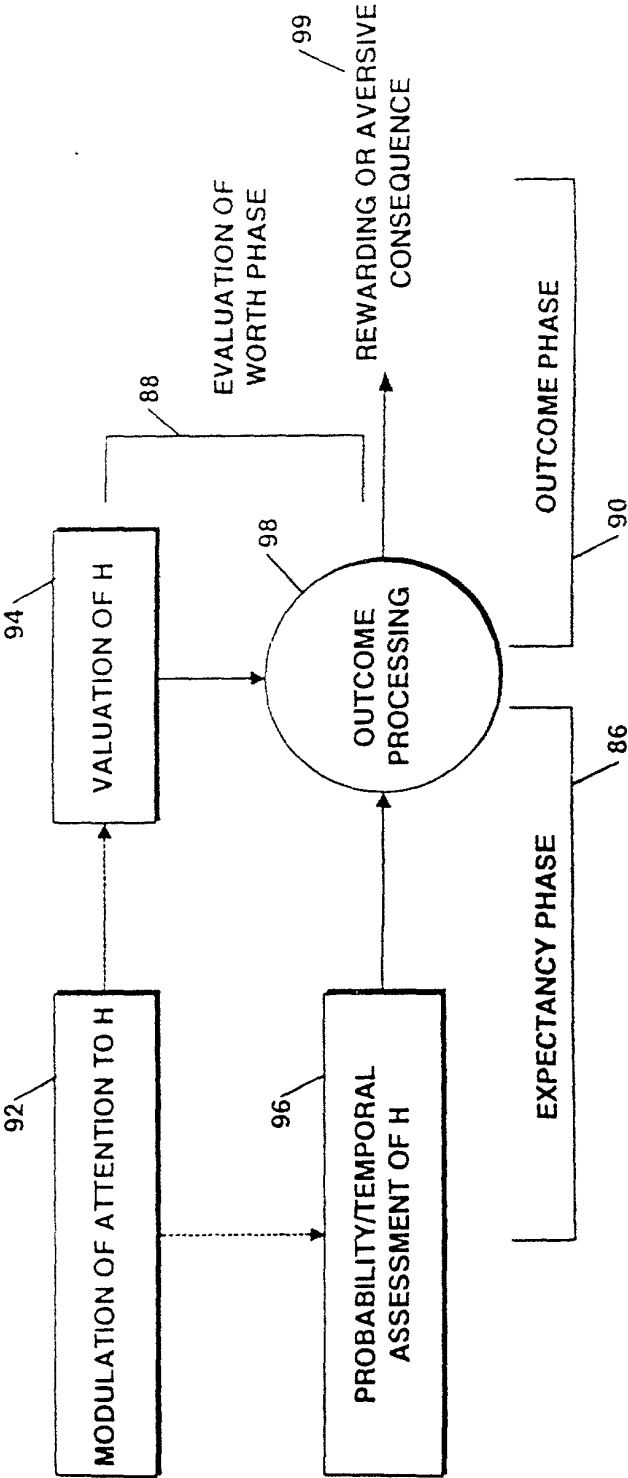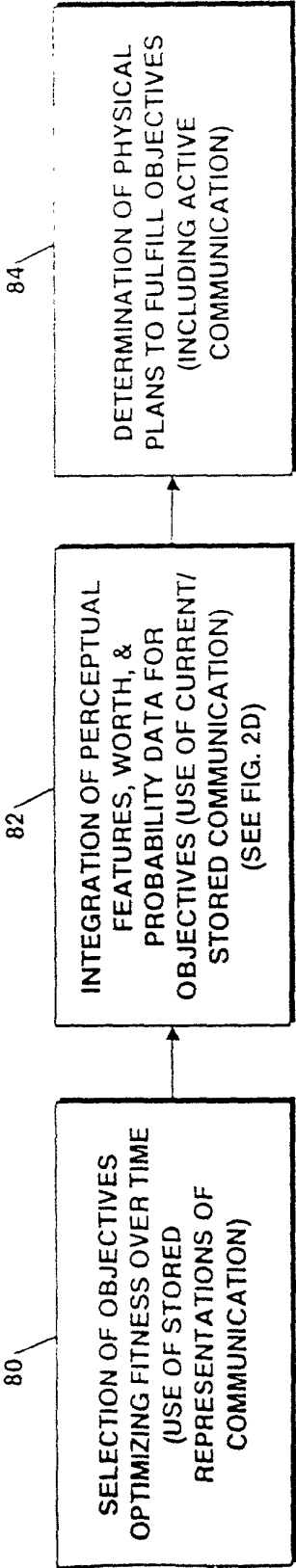Lino Becerra, Et Al.
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Figure 2A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
CASE NO. MGH-004BUS

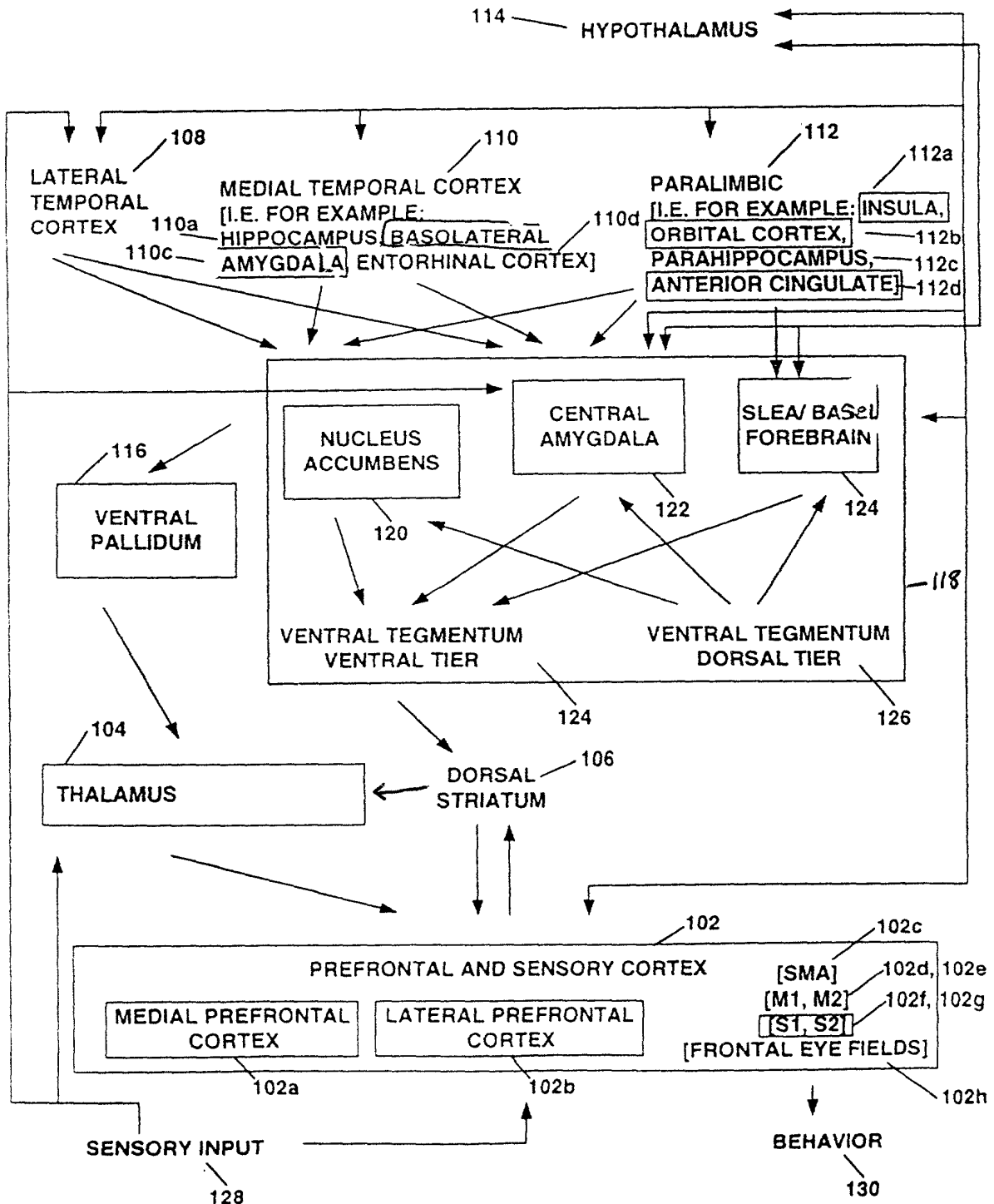3/41

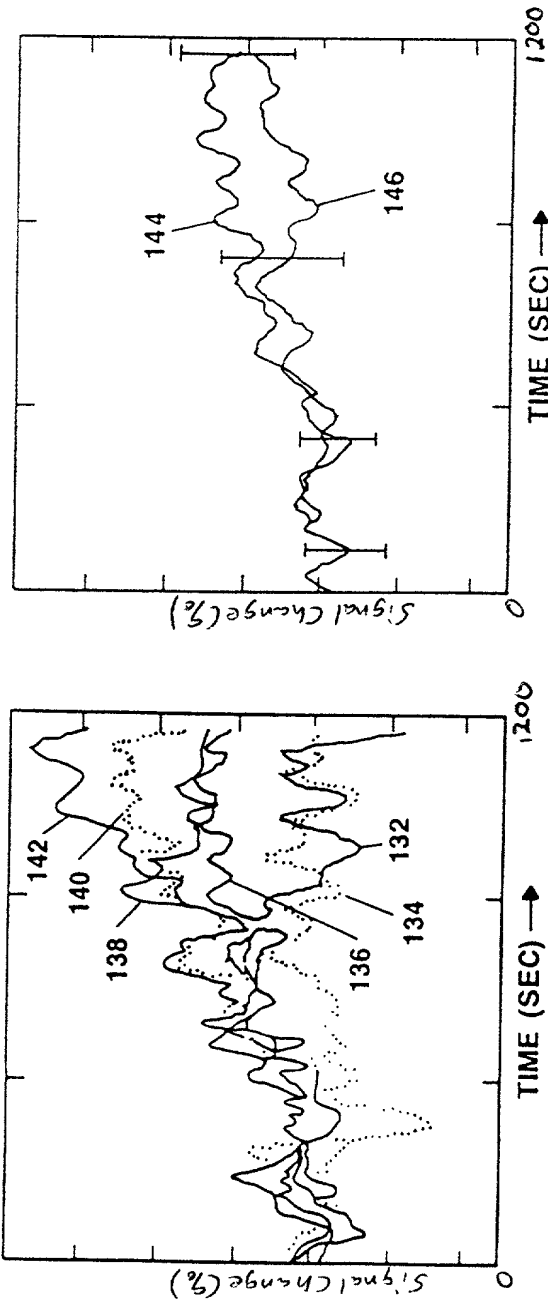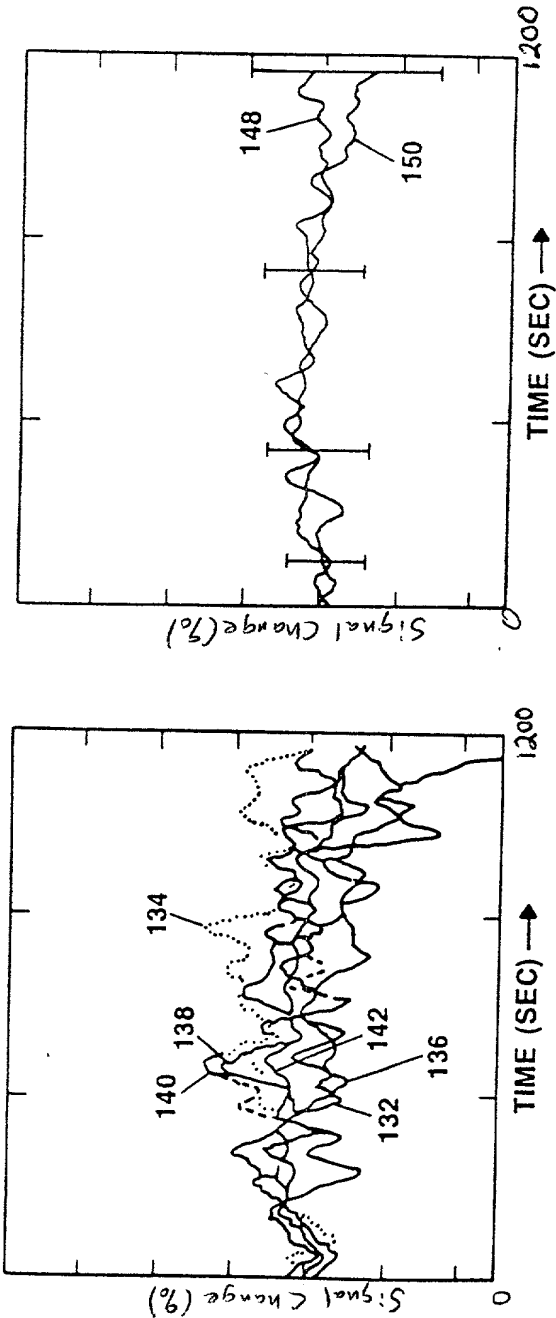*Figure 2B*

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Figure 2C

80 — SELECTION OF OBJECTIVES OPTIMIZING FITNESS OVER TIME (USE OF STORED REPRESENTATIONS OF COMMUNICATION)

82 — INTEGRATION OF PERCEPTUAL FEATURES, WORTH, & PROBABILITY DATA FOR OBJECTIVES (USE OF CURRENT/ STORED COMMUNICATION) (SEE FIG. 2D)

84 — DETERMINATION OF PHYSICAL PLANS TO FULFILL OBJECTIVES (INCLUDING ACTIVE COMMUNICATION)

Figure 2D

92 — MODULATION OF ATTENTION TO H

94 — VALUATION OF H

96 — PROBABILITY/TEMPORAL ASSESSMENT OF H

98 — OUTCOME PROCESSING

88 — EVALUATION OF WORTH PHASE

99 — REWARDING OR AVERSIVE CONSEQUENCE

86 — EXPECTANCY PHASE

90 — OUTCOME PHASE

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
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Figure 3

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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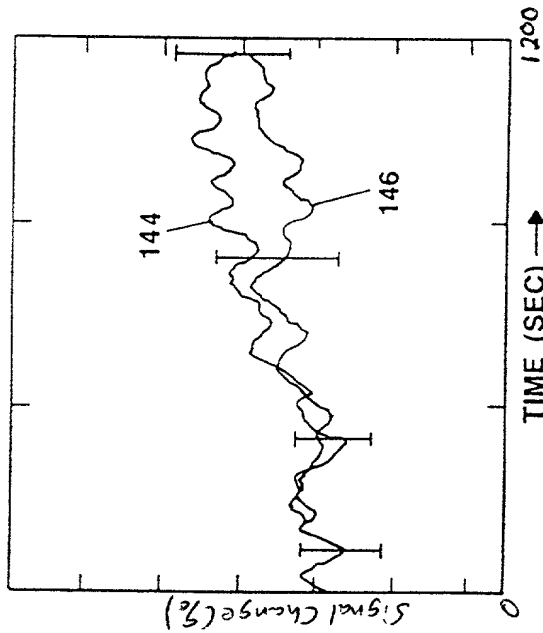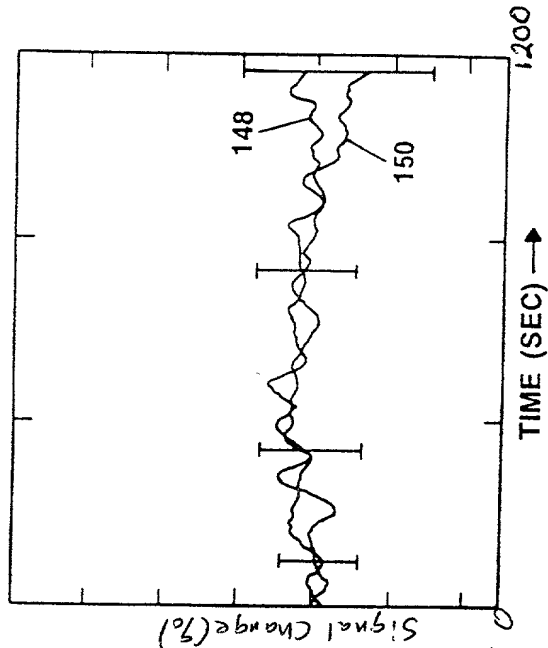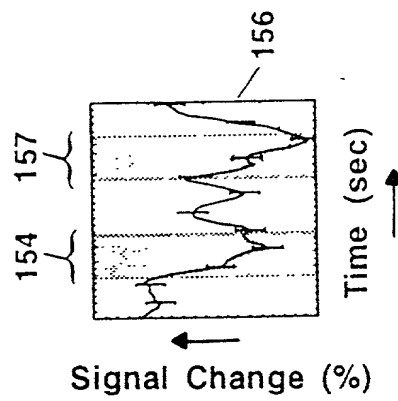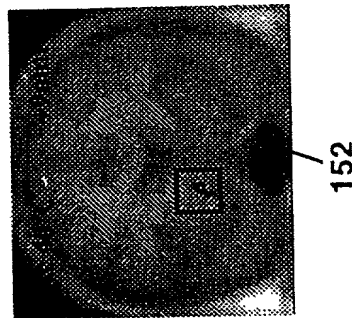6/41

Figure 3C

Figure 3D
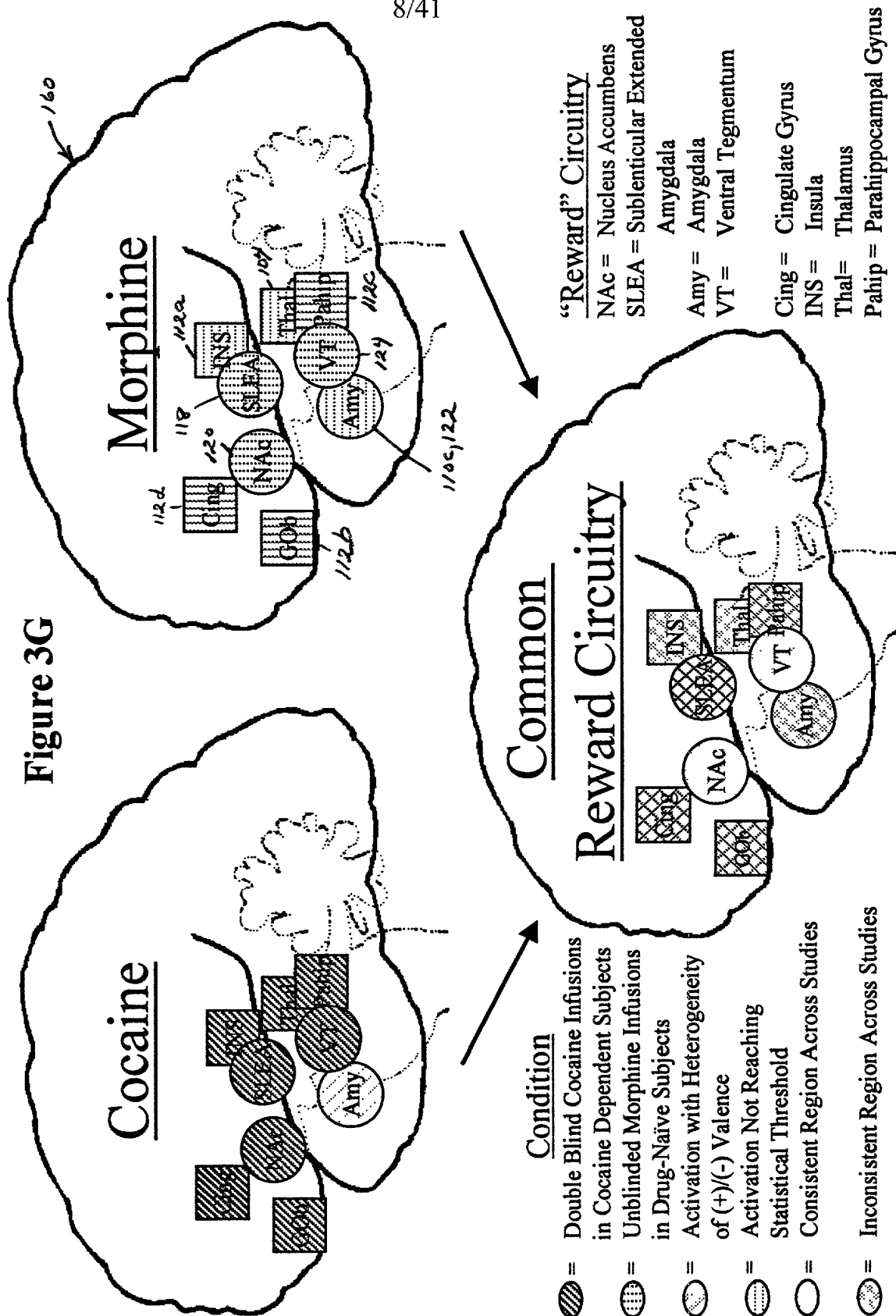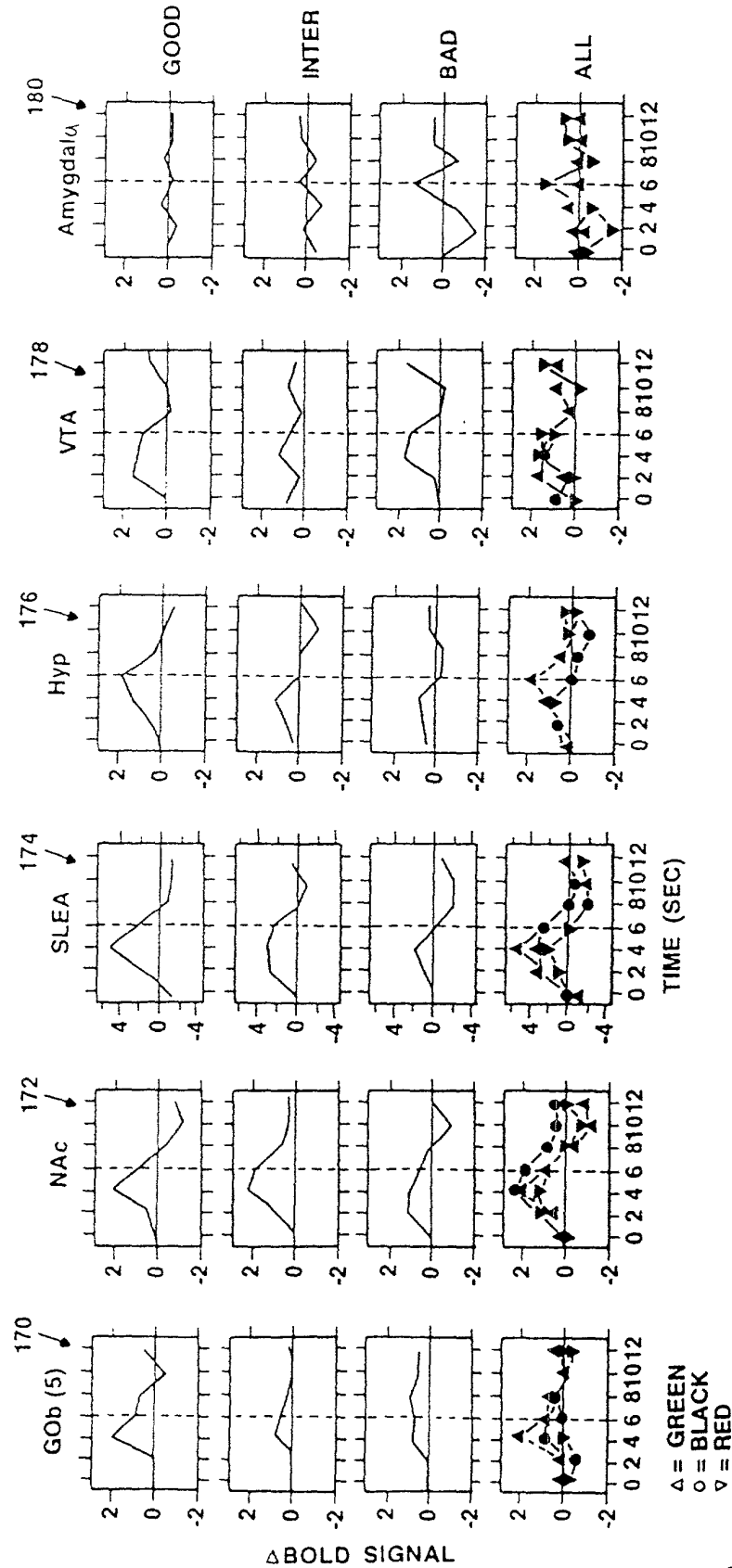
Figure 3A

Figure 3B

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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Figure 3F

Figure 3E

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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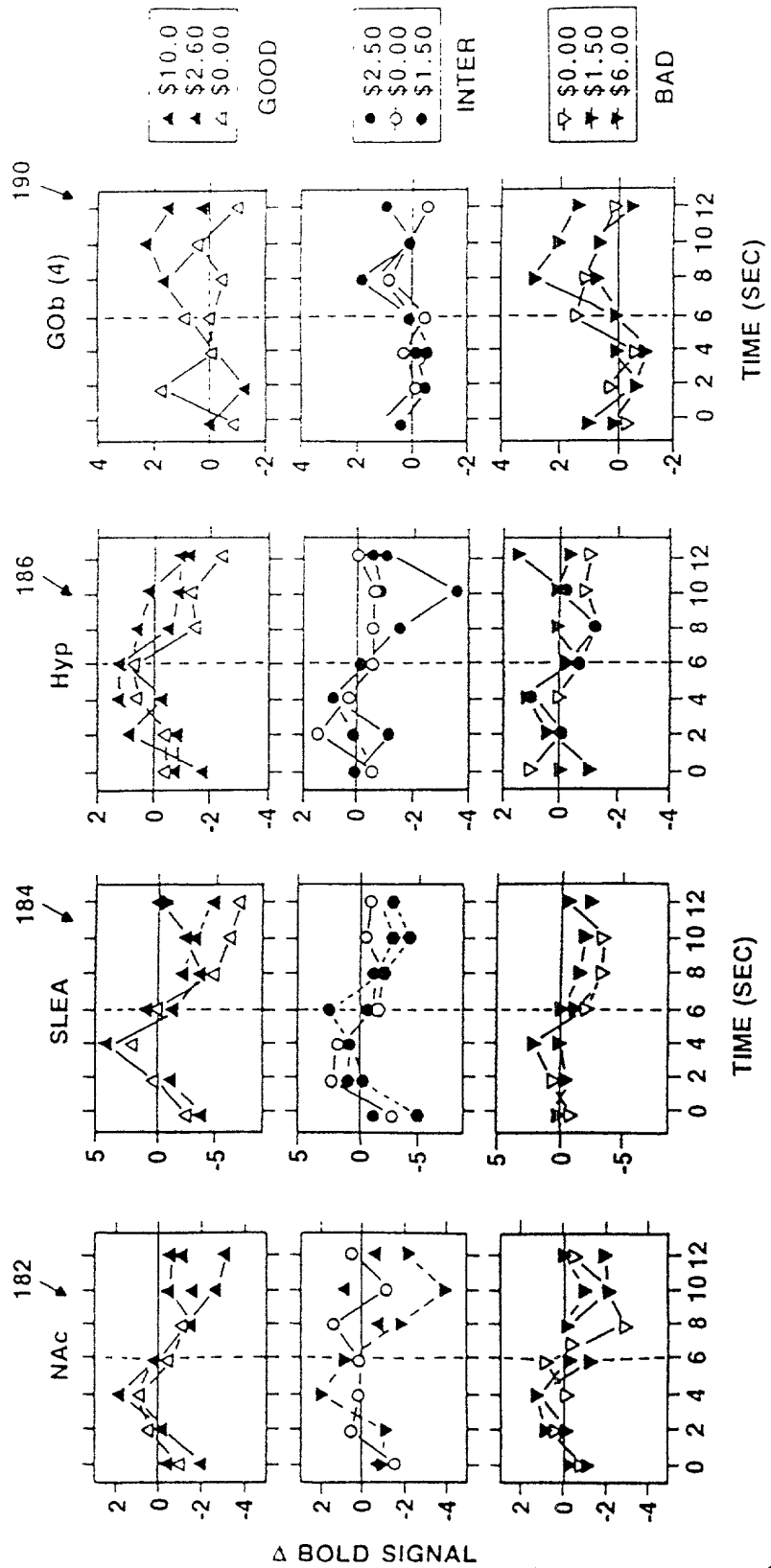
Figure 3G

"Reward" Circuitry
NAc = Nucleus Accumbens
SLEA = Sublenticular Extended Amygdala
Amy = Amygdala
VT = Ventral Tegmentum
Cing = Cingulate Gyrus
INS = Insula
Thal = Thalamus
Pahip = Parahippocampal Gyrus

Condition
= Double Blind Cocaine Infusions in Cocaine Dependent Subjects
= Unblinded Morphine Infusions in Drug-Naive Subjects
= Activation with Heterogeneity of (+)/(−) Valence
= Activation Not Reaching Statistical Threshold
= Consistent Region Across Studies
= Inconsistent Region Across Studies

Figure 3H

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
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Figure 3I

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
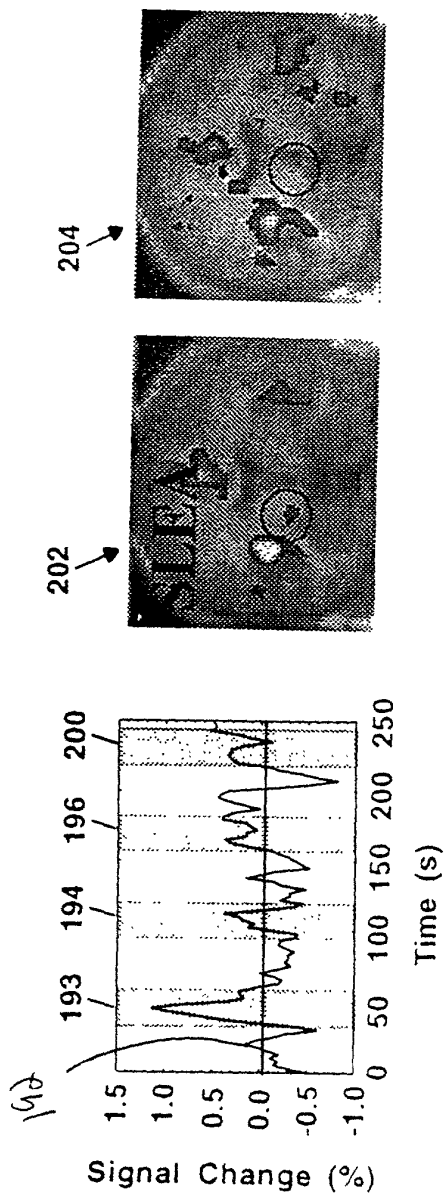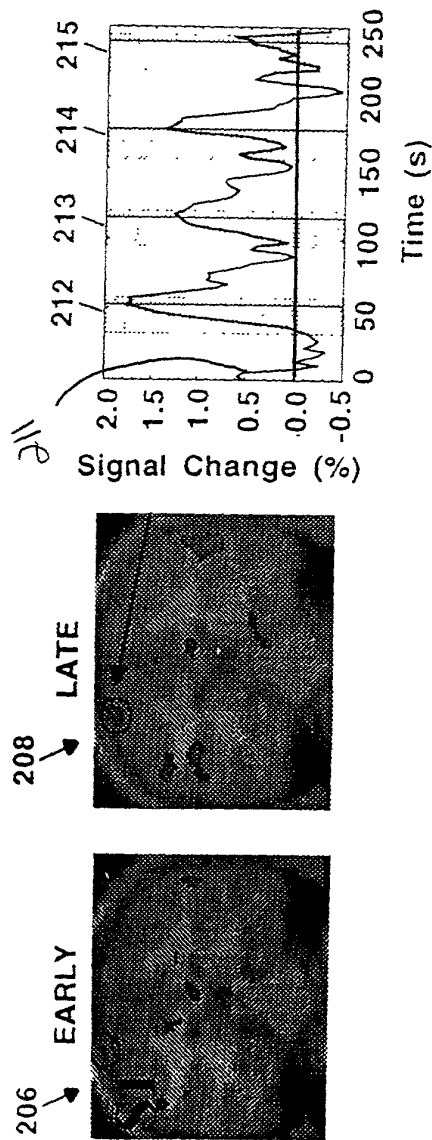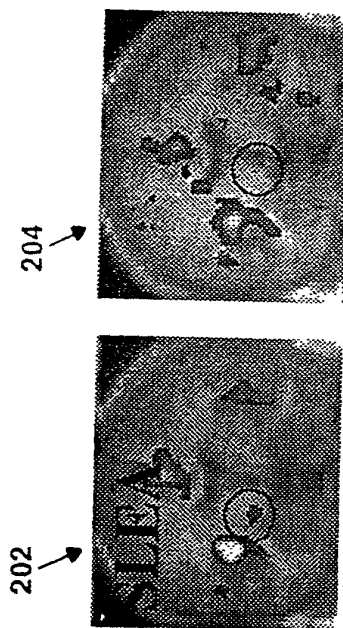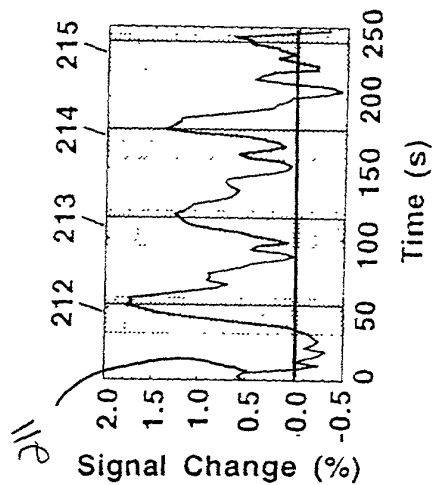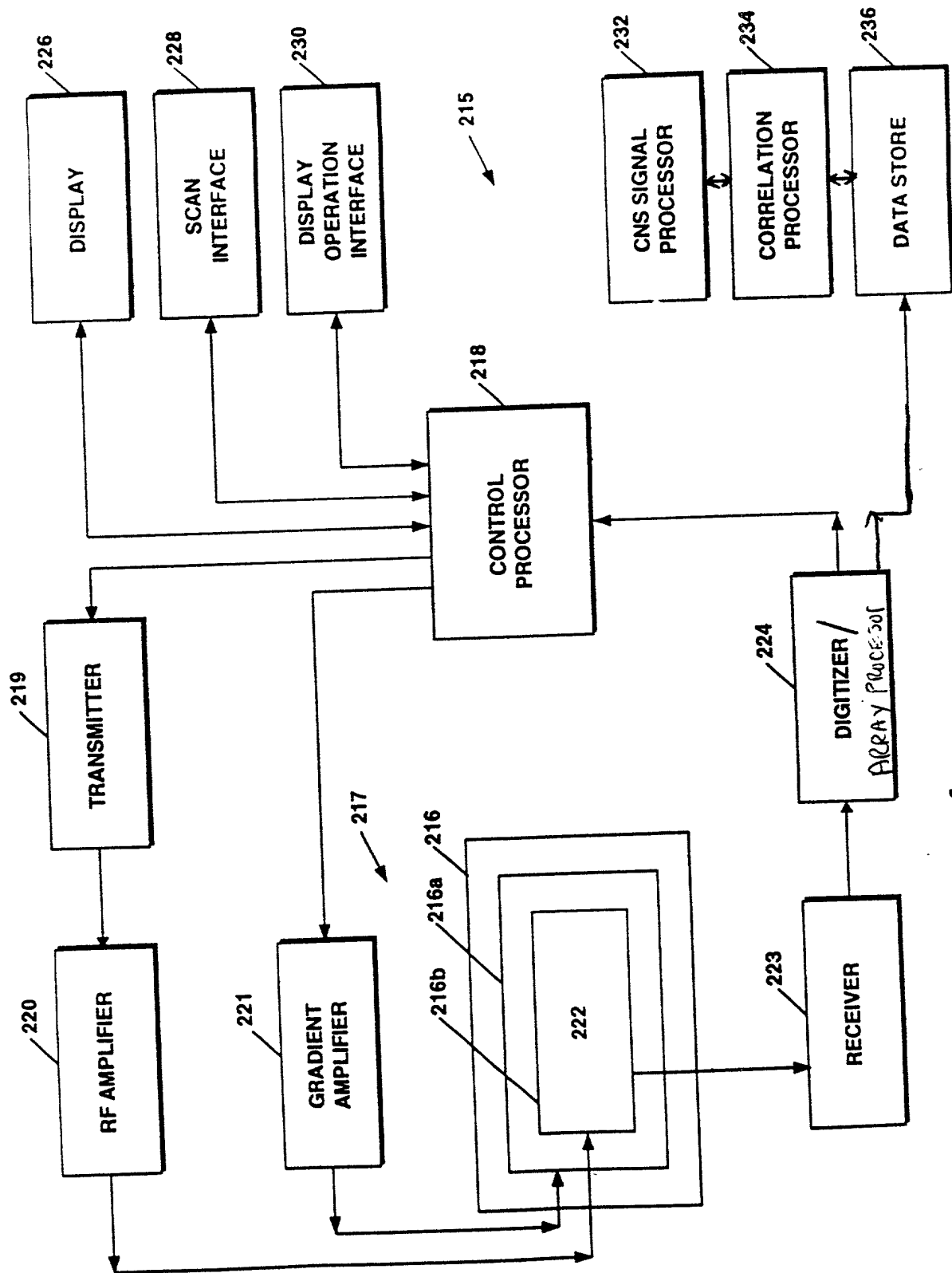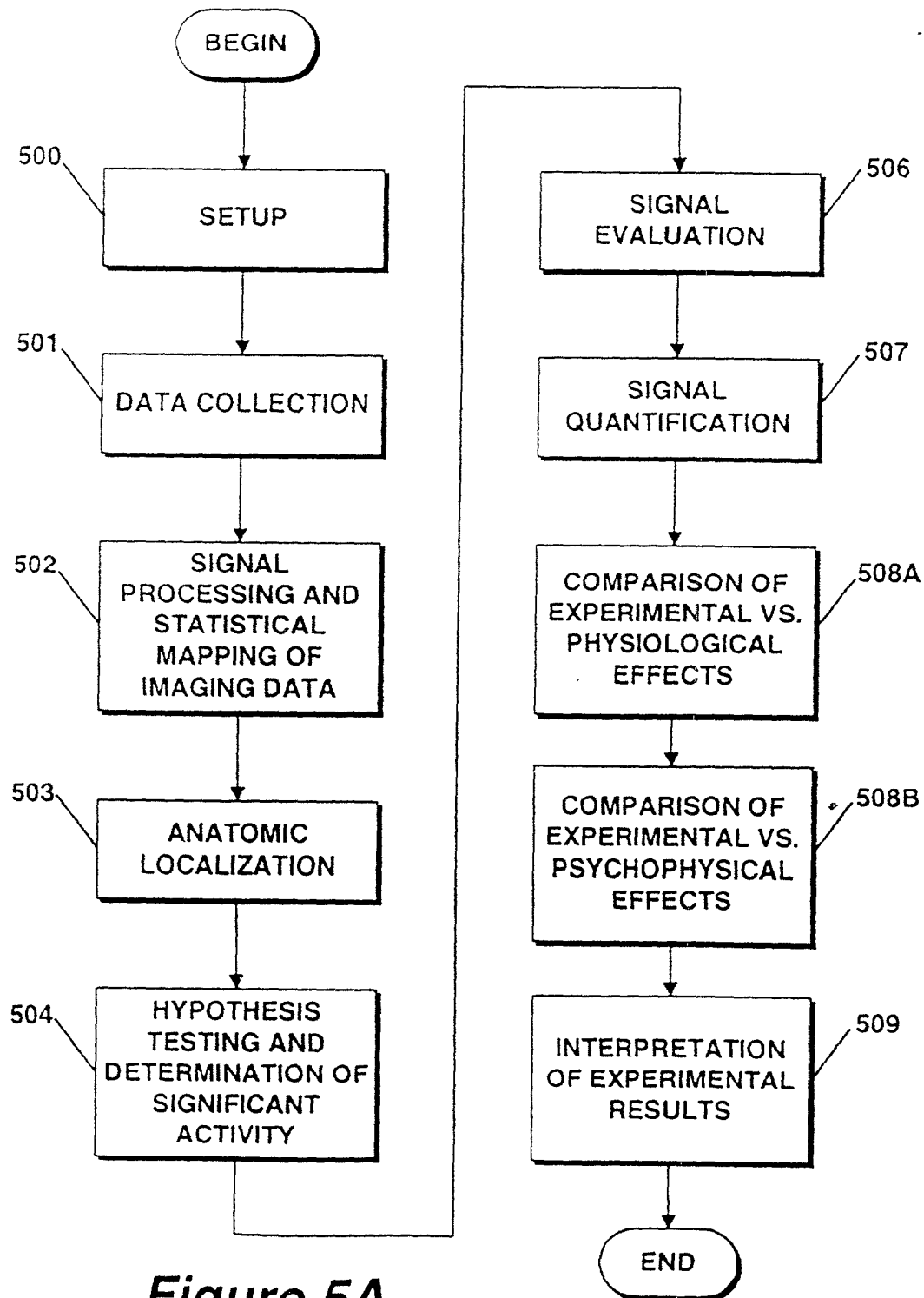CASE NO. MGH-004BUS

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Figure 3K   Figure 3L

Figure 3J

Figure 3M   Figure 3N

Figure 3O

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
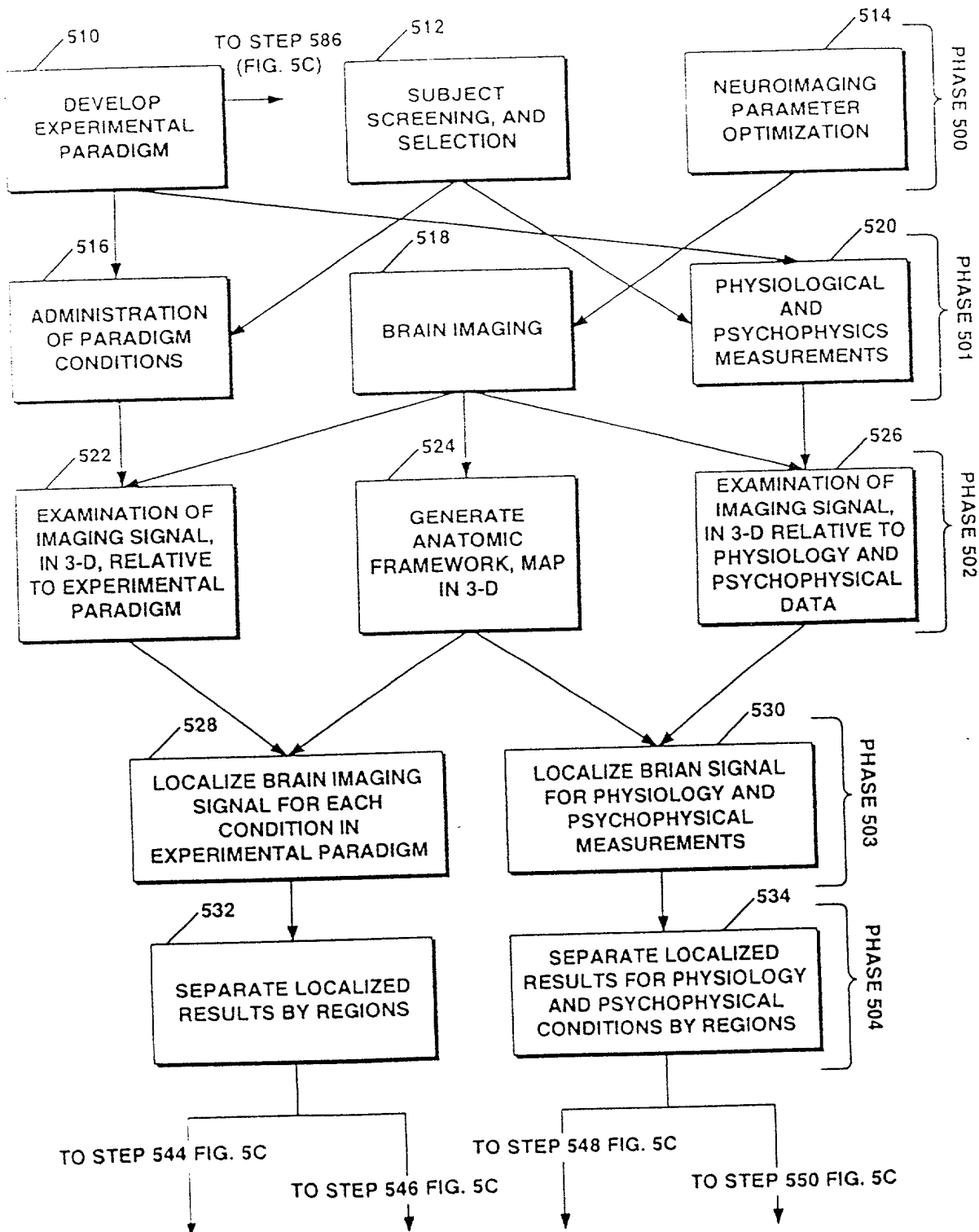Lino Becerra, Et Al.
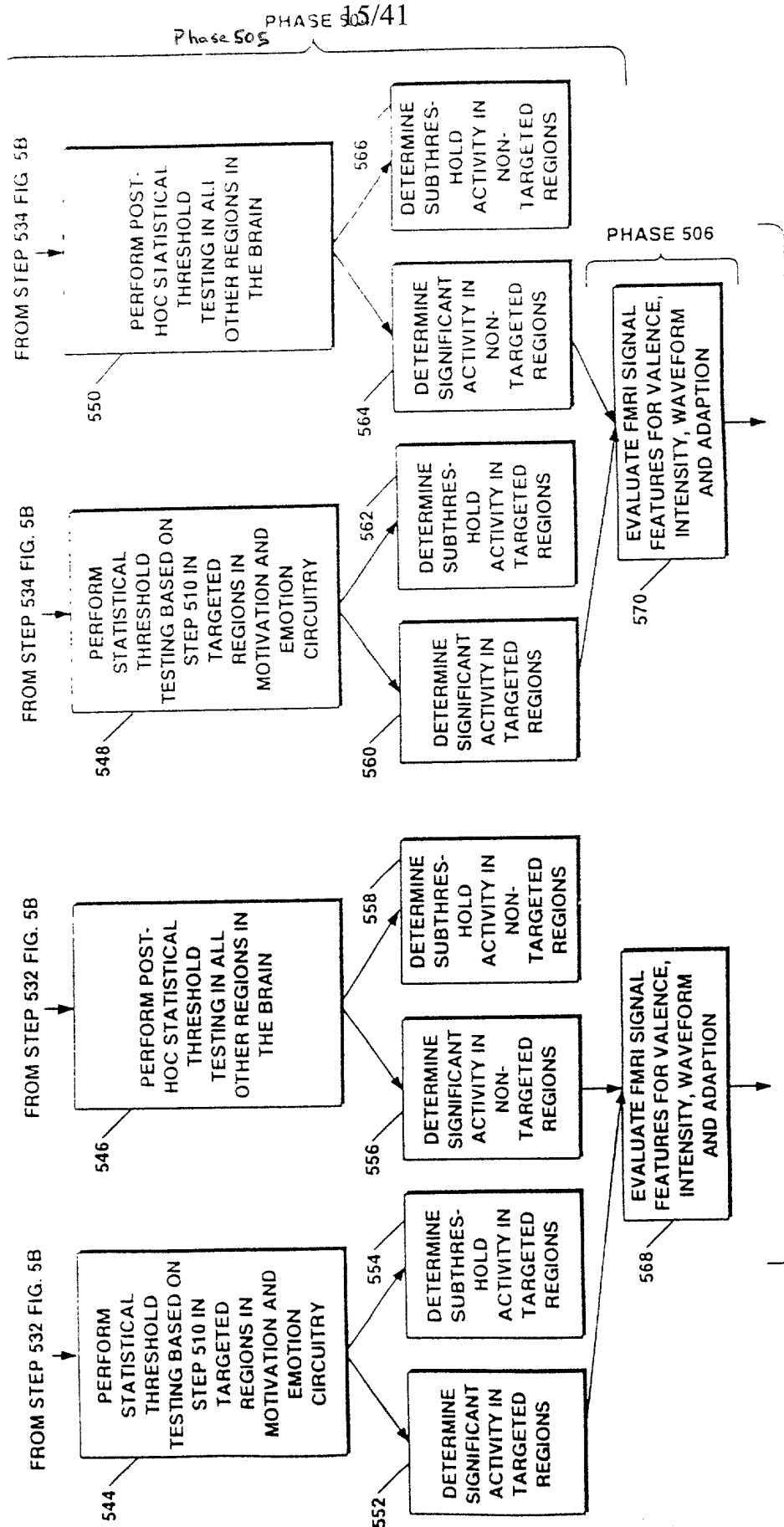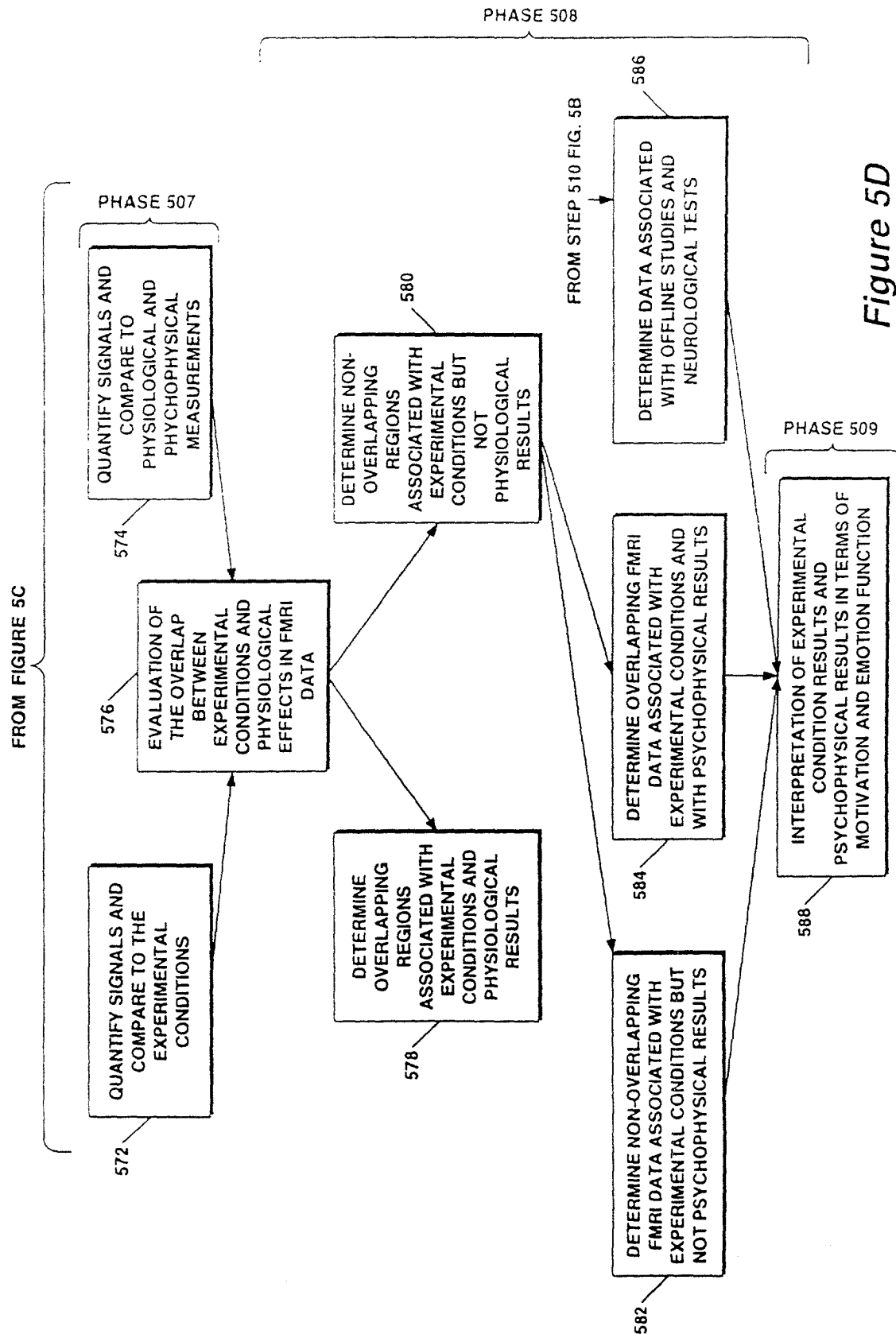CASE NO. MGH-004BUS

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Figure 4

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
CASE NO. MGH-004BUS

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```
                    ┌─────────┐
                    │  BEGIN  │
                    └─────────┘
                         │
  500                    ▼                          ▼                      506
        ┌─────────────────────┐      ┌─────────────────────┐
        │       SETUP         │      │      SIGNAL          │
        │                     │      │    EVALUATION        │
        └─────────────────────┘      └─────────────────────┘
                  │                             │
  501             ▼                             ▼               507
        ┌─────────────────────┐      ┌─────────────────────┐
        │  DATA COLLECTION    │      │      SIGNAL          │
        │                     │      │  QUANTIFICATION      │
        └─────────────────────┘      └─────────────────────┘
                  │                             │
  502             ▼                             ▼               508A
        ┌─────────────────────┐      ┌─────────────────────┐
        │      SIGNAL         │      │  COMPARISON OF       │
        │  PROCESSING AND     │      │  EXPERIMENTAL VS.    │
        │   STATISTICAL       │      │  PHYSIOLOGICAL       │
        │   MAPPING OF        │      │     EFFECTS          │
        │  IMAGING DATA       │      └─────────────────────┘
        └─────────────────────┘                 │
                  │                              ▼               508B
  503             ▼                   ┌─────────────────────┐
        ┌─────────────────────┐      │  COMPARISON OF       │
        │     ANATOMIC        │      │  EXPERIMENTAL VS.    │
        │   LOCALIZATION      │      │  PSYCHOPHYSICAL      │
        │                     │      │     EFFECTS          │
        └─────────────────────┘      └─────────────────────┘
                  │                              │
  504             ▼                              ▼               509
        ┌─────────────────────┐      ┌─────────────────────┐
        │    HYPOTHESIS       │      │  INTERPRETATION      │
        │   TESTING AND       │      │  OF EXPERIMENTAL     │
        │ DETERMINATION OF    │      │     RESULTS          │
        │   SIGNIFICANT       │      └─────────────────────┘
        │    ACTIVITY         │                 │
        └─────────────────────┘                 ▼
                  │                         ┌─────────┐
                  └──────────────────────  │   END   │
                                           └─────────┘
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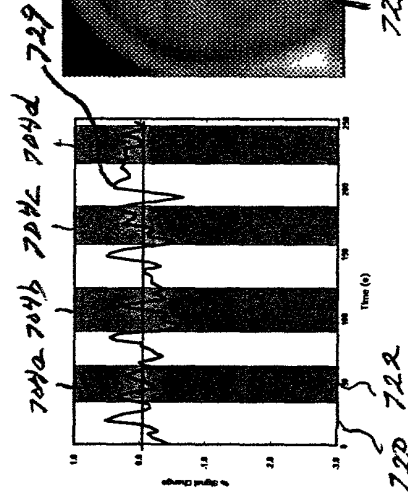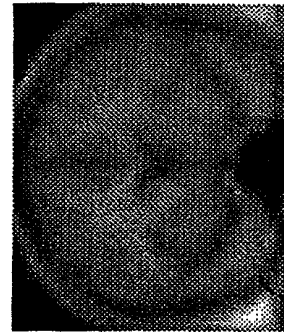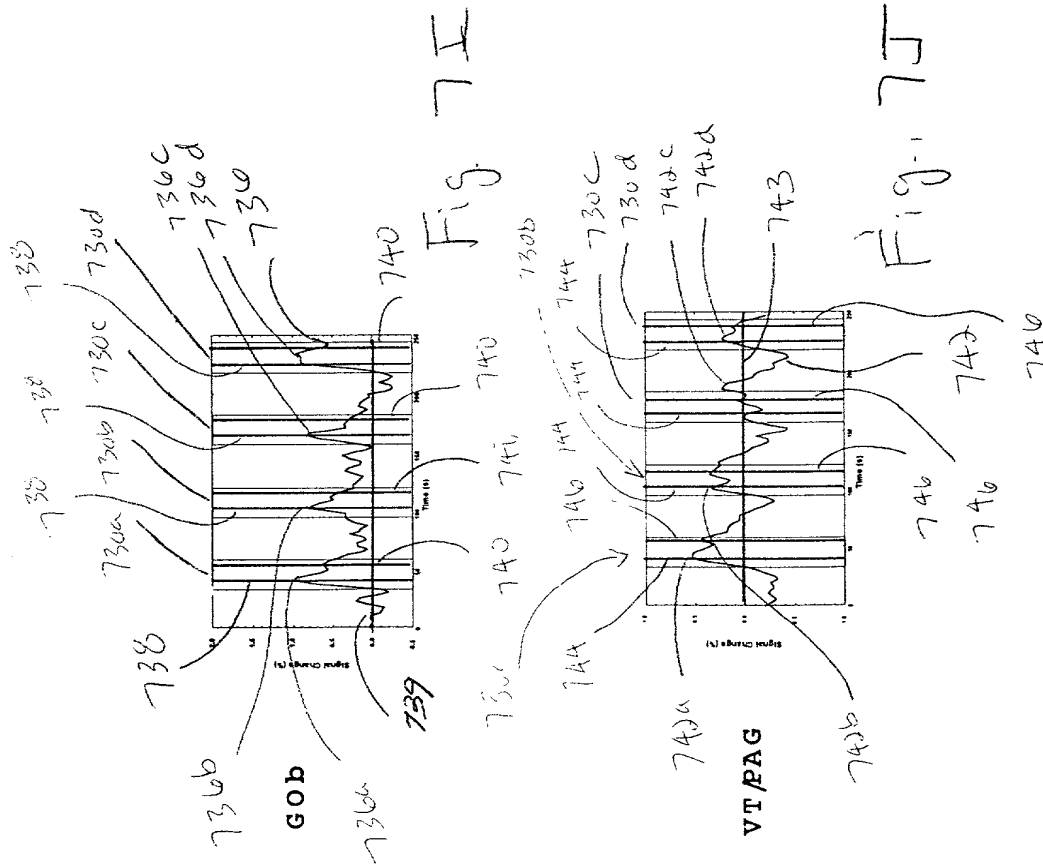
Figure 5A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
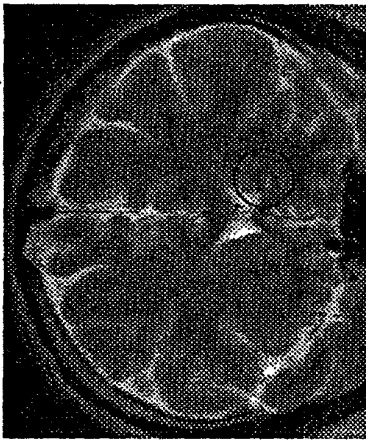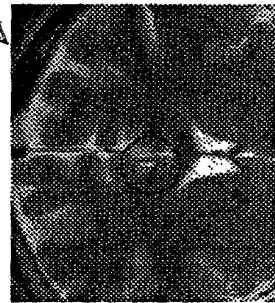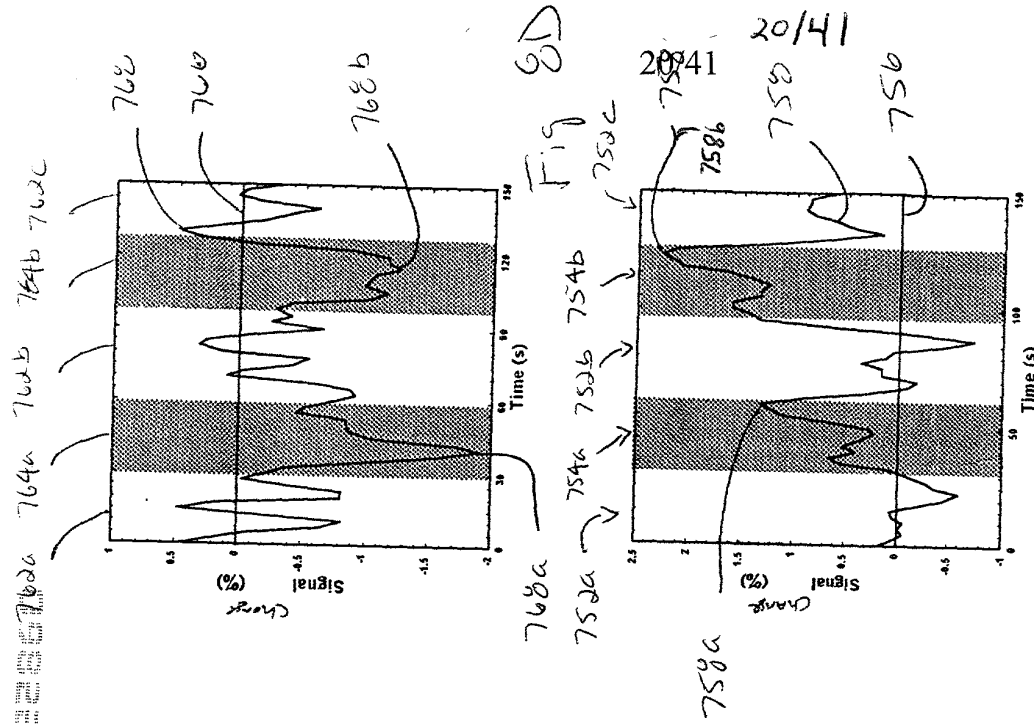Lino Becerra, Et Al.
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Figure 5B

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
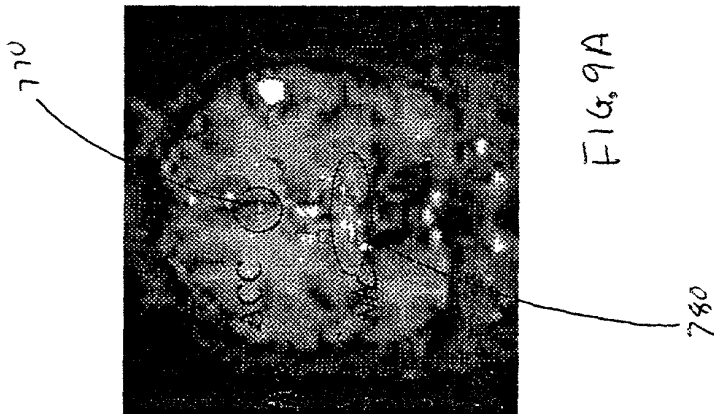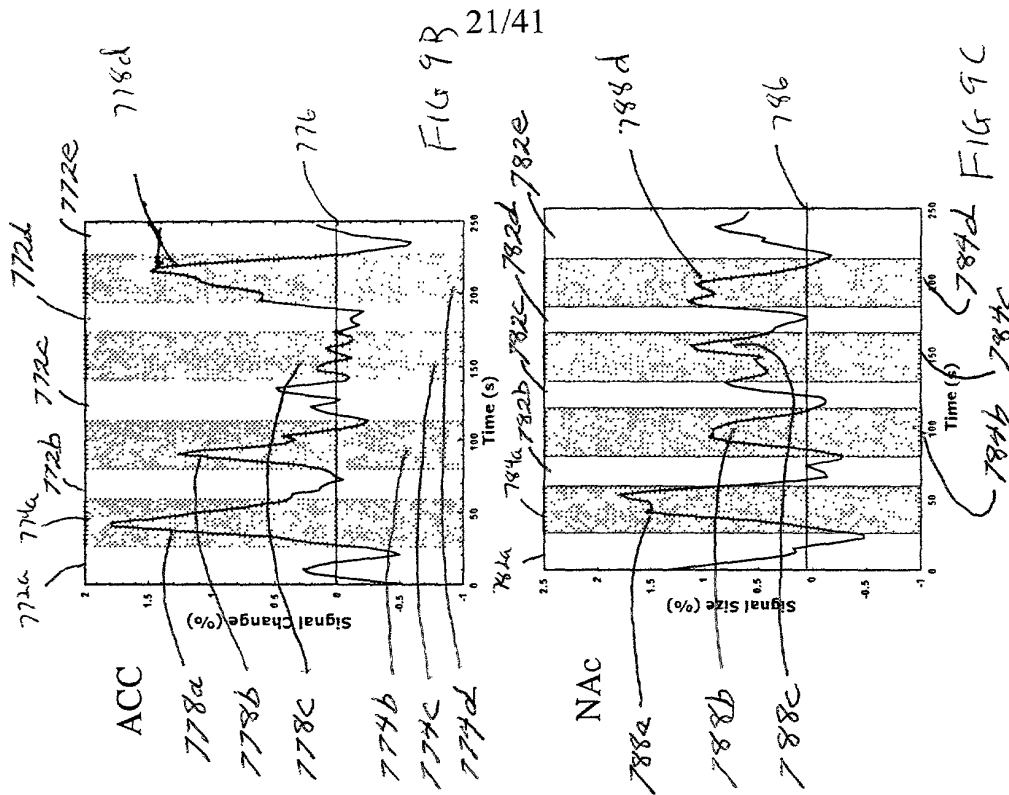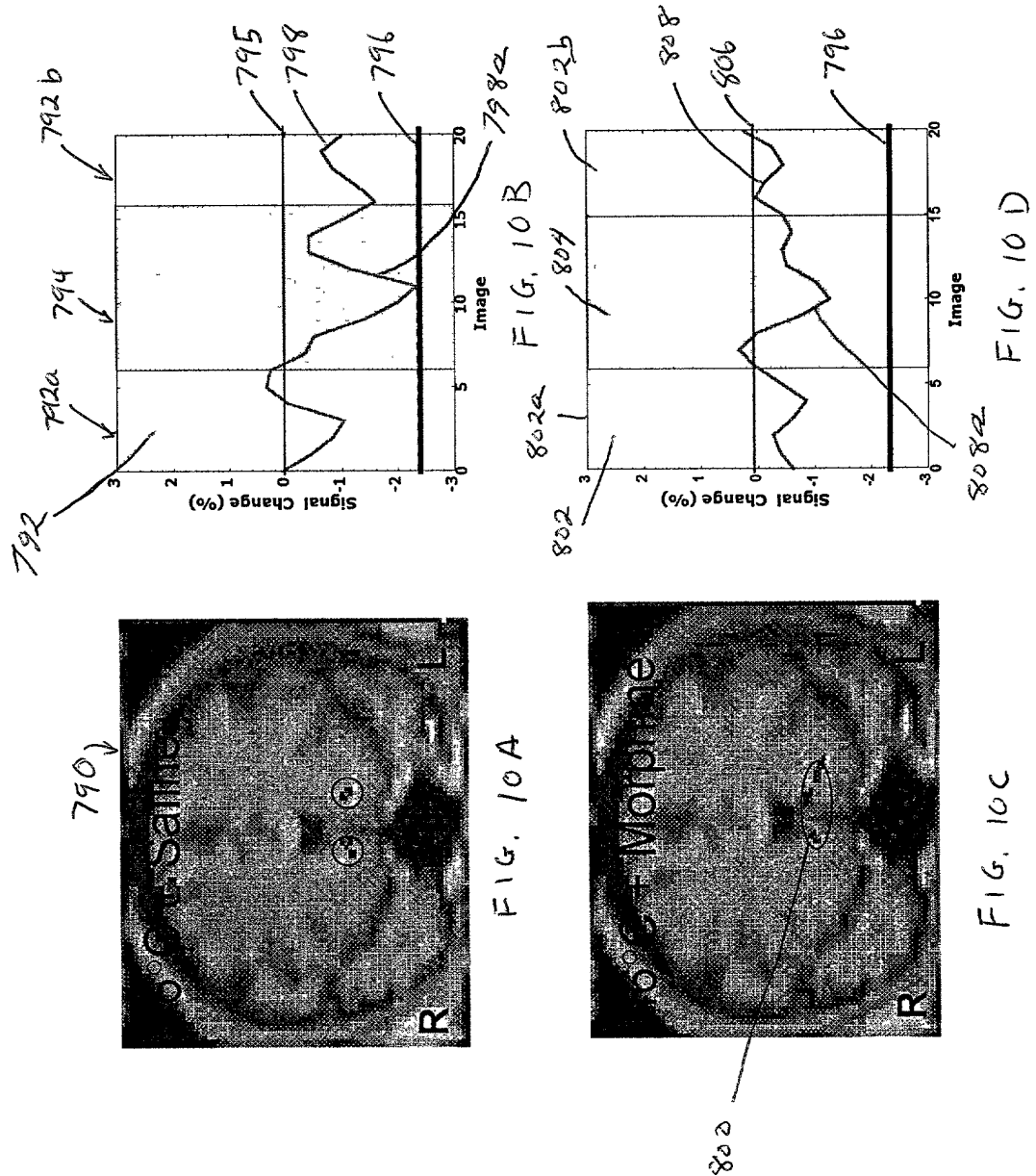Lino Becerra, Et Al.
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Figure 5C

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
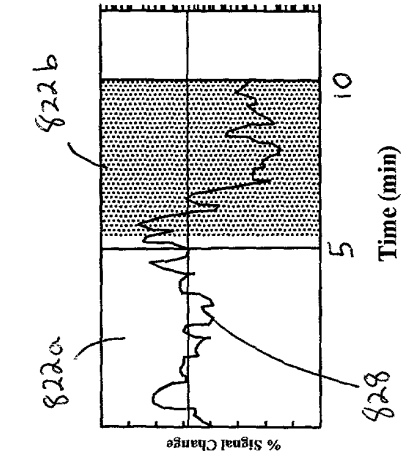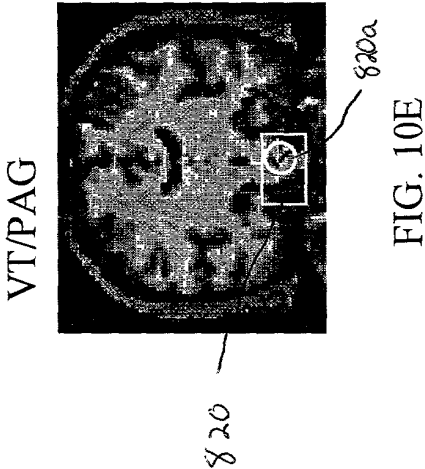Lino Becerra, Et Al.
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Figure 5D

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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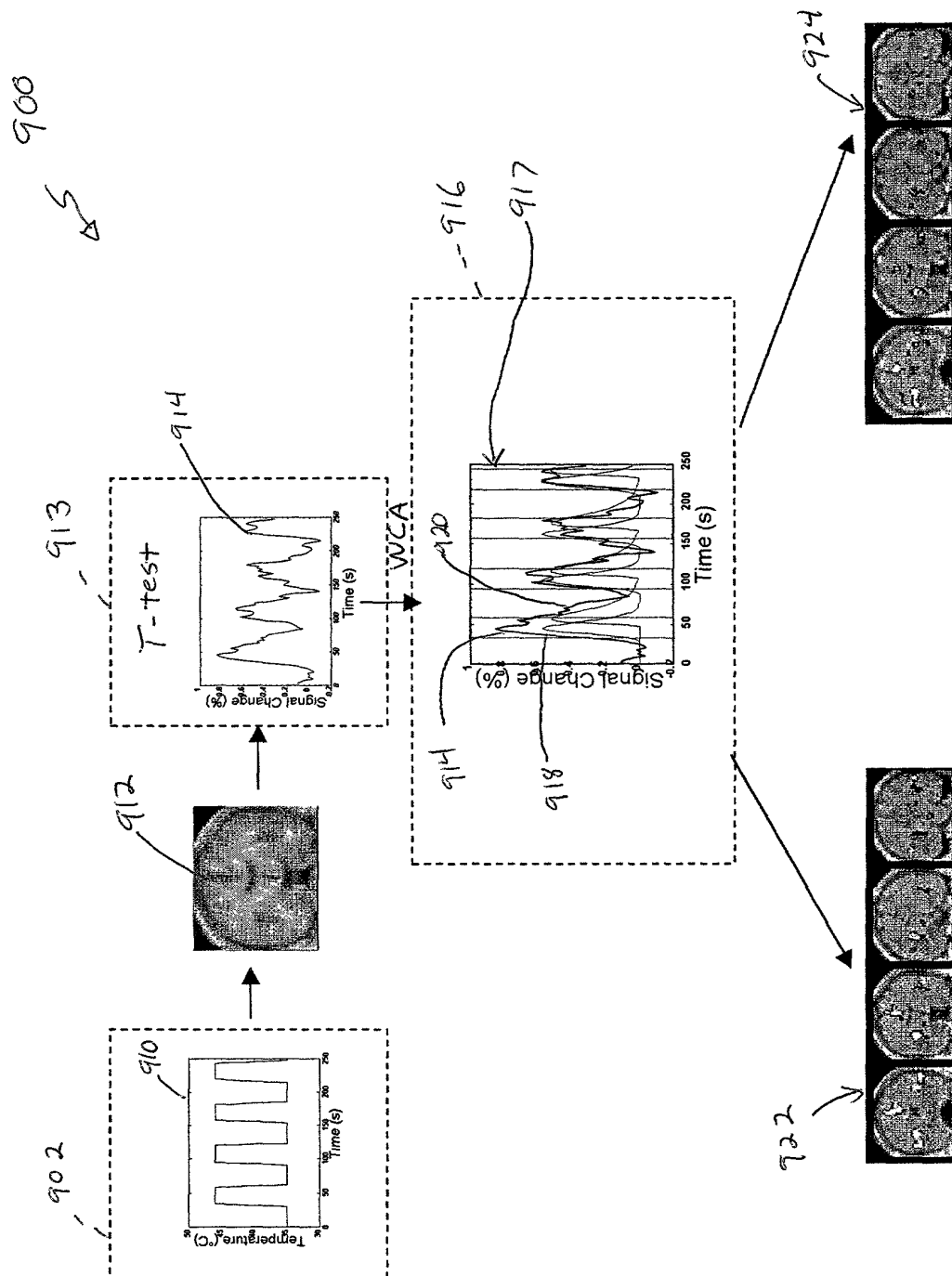
Figure 6
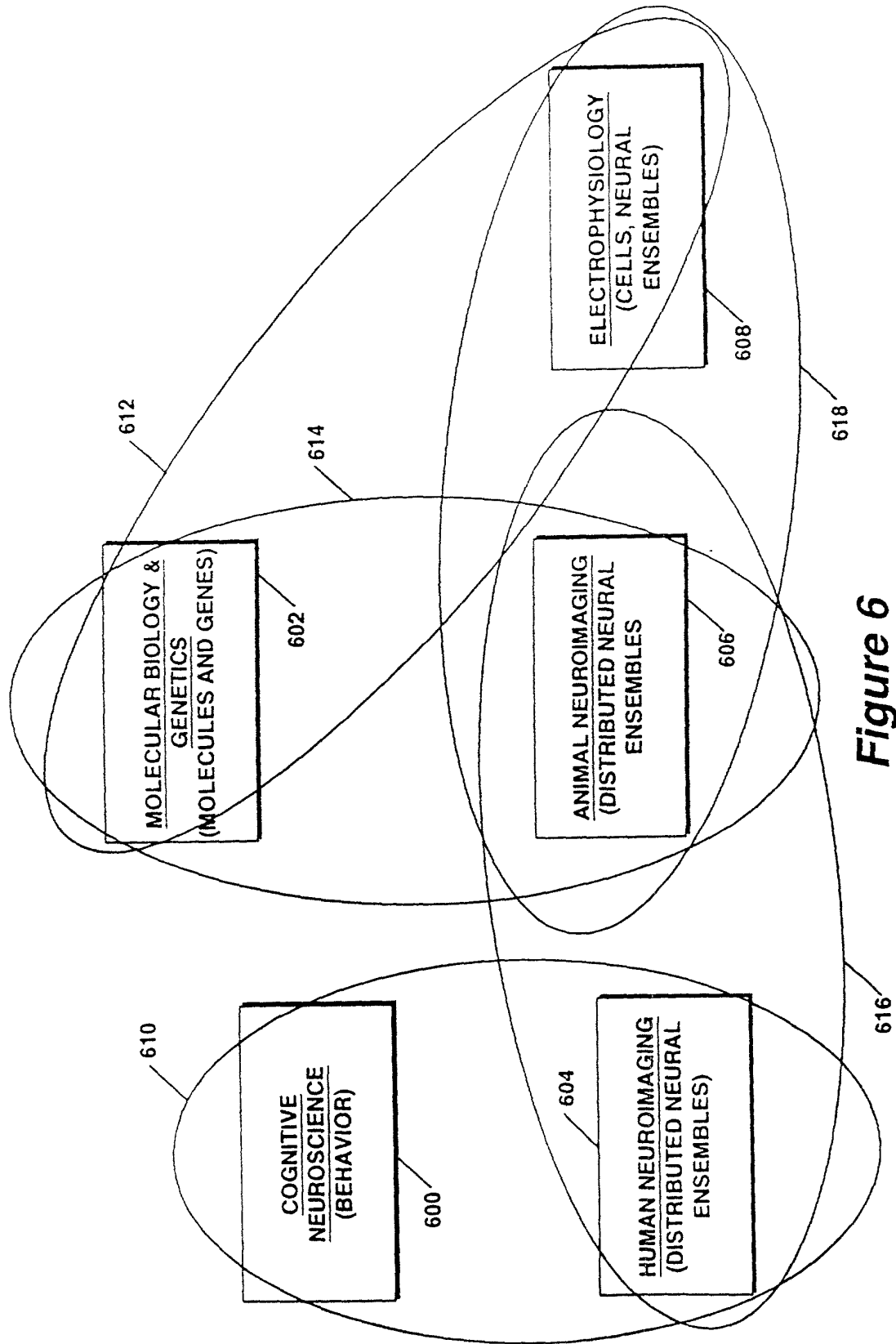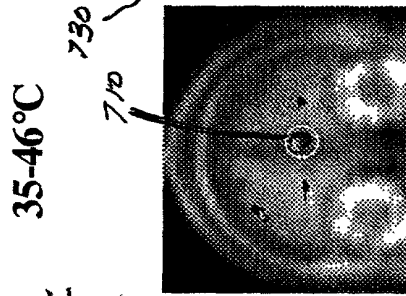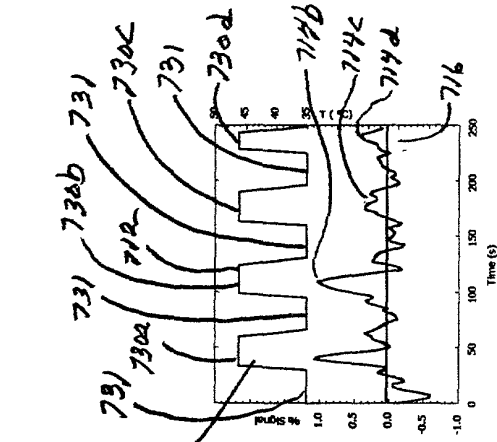
METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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FIG. 7A
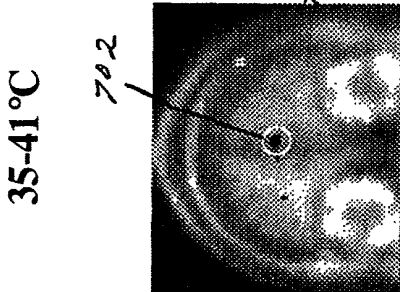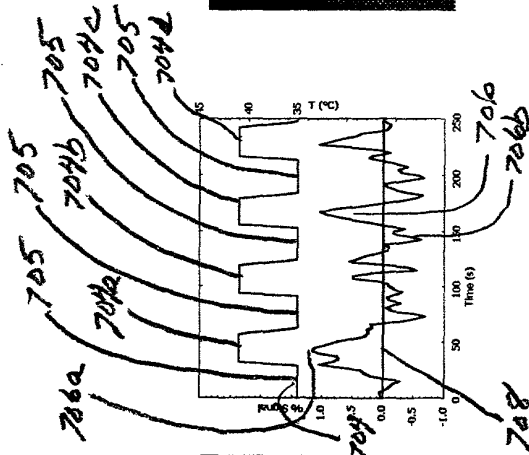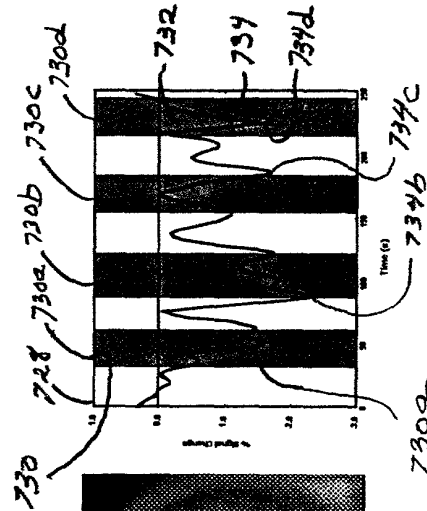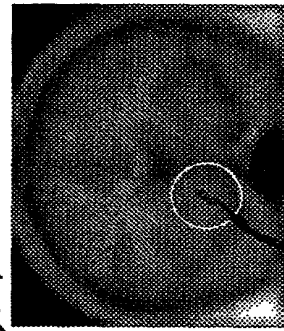
FIG. 7B

FIG. 7C

FIG. 7D

FIG. 7E

FIG. 7F

FIG. 7G

FIG. 7H

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Fig. H

Fig. I

Figure 8B

Figure 8C

Figure 8A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
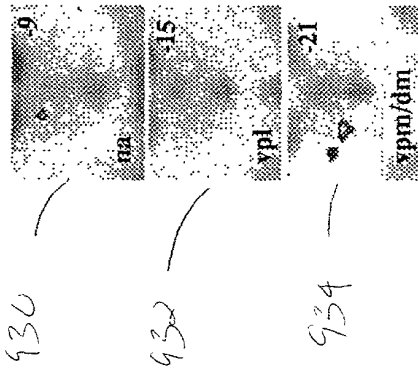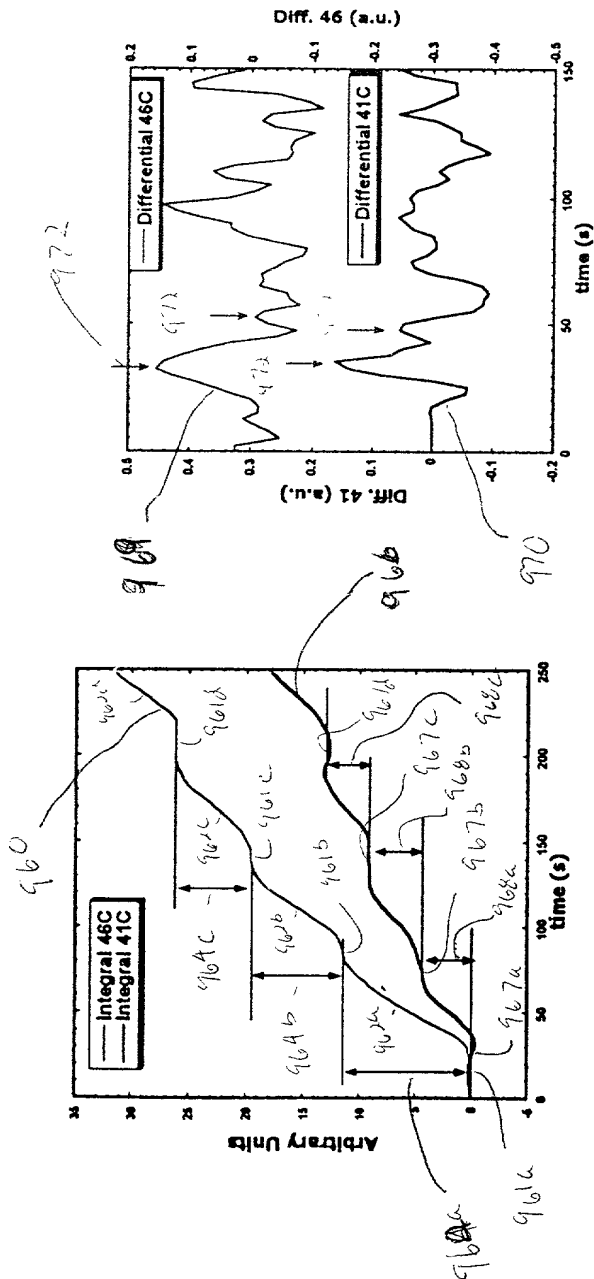Lino Becerra, Et Al.
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FIG 9B

FIG 9C

FIG. 9A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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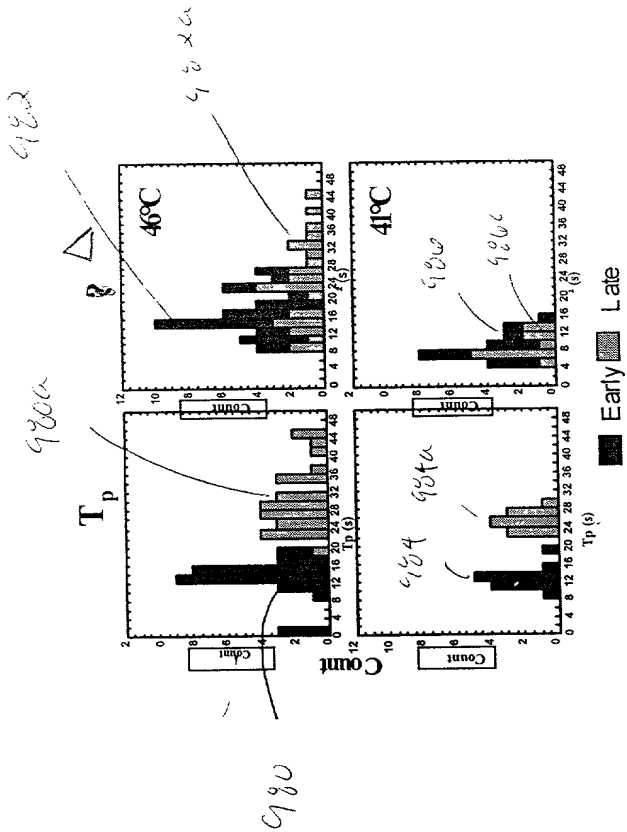FIG. 10A

FIG. 10B

FIG. 10C

FIG. 10D

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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VT/PAG

FIG. 10E

FIG. 10F

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
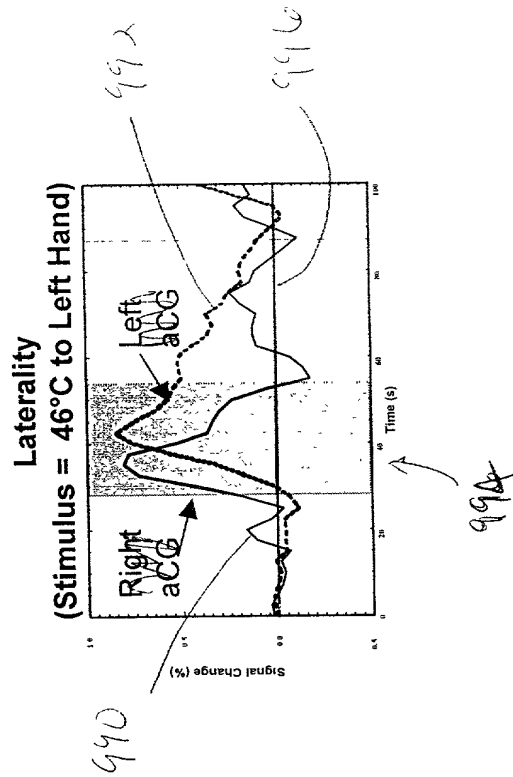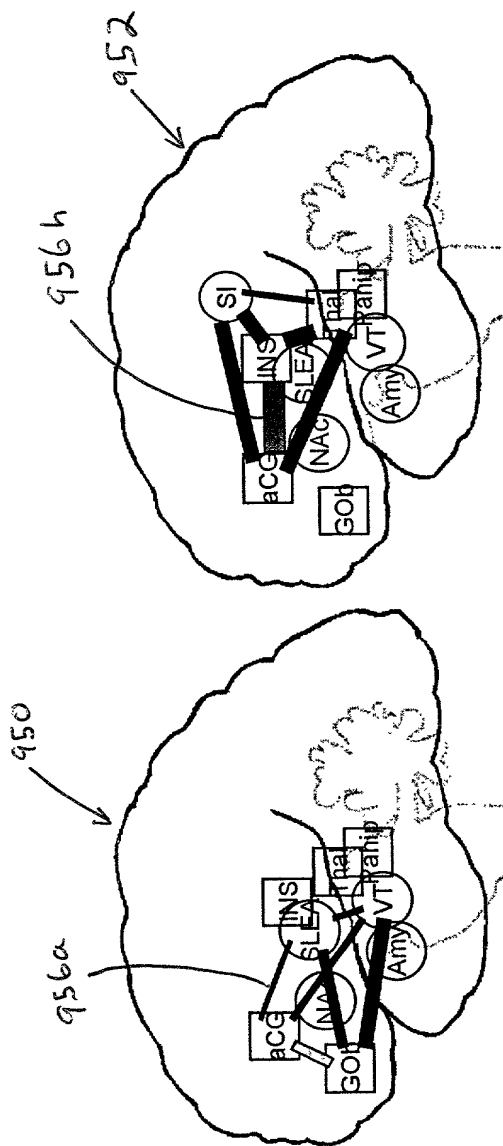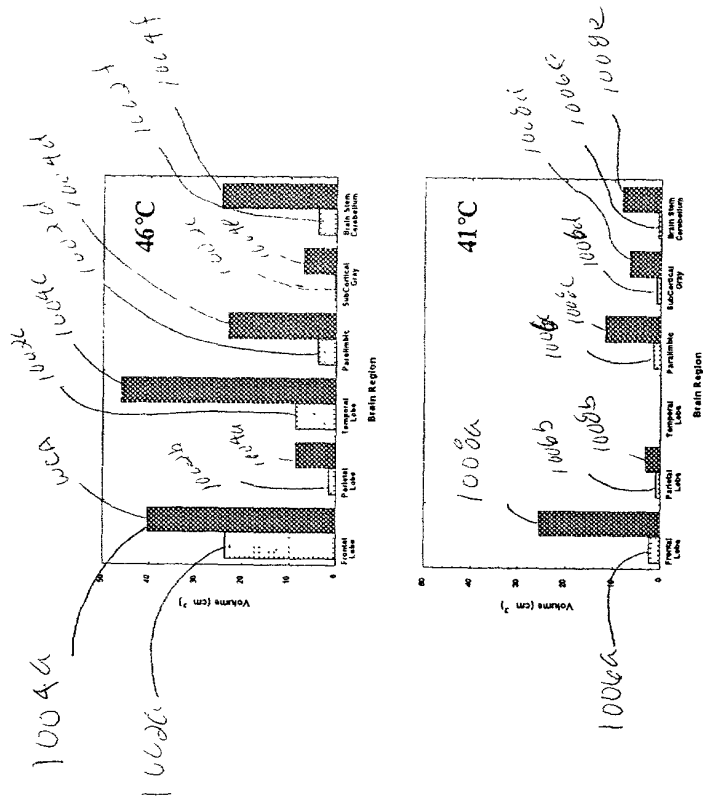Lino Becerra, Et Al.
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Figure 11

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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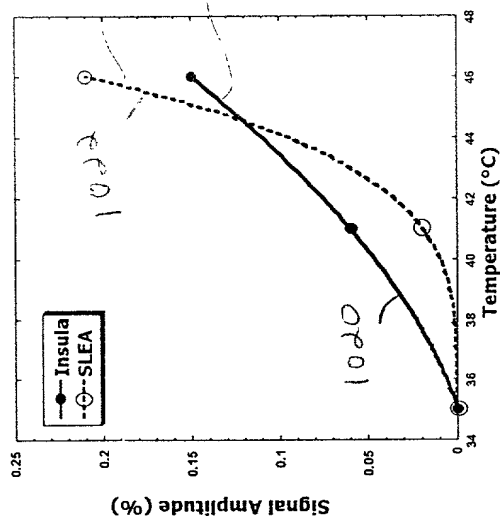FIG. 11A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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FIG. 11C

FIG. 11B

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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Figure 11D

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
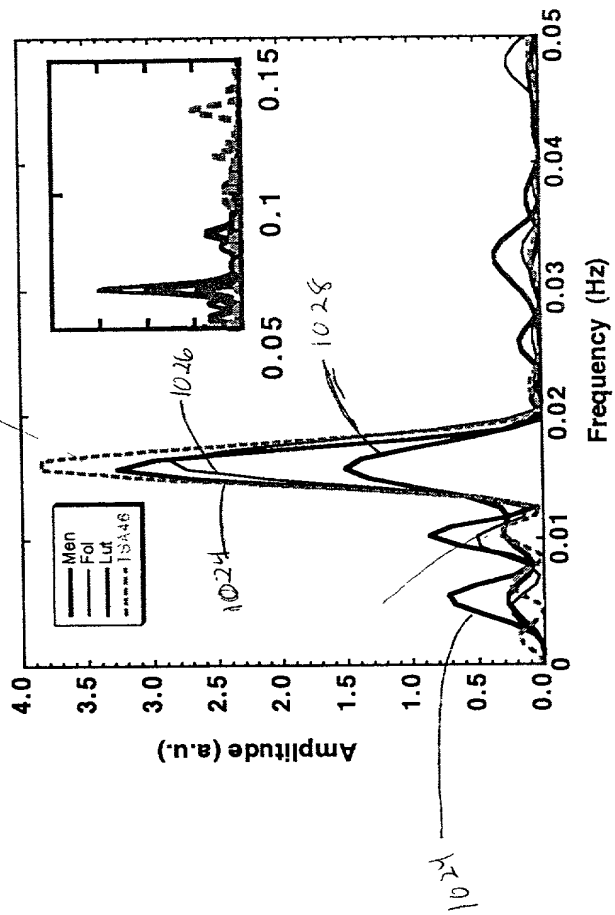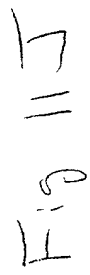Lino Becerra, Et Al.
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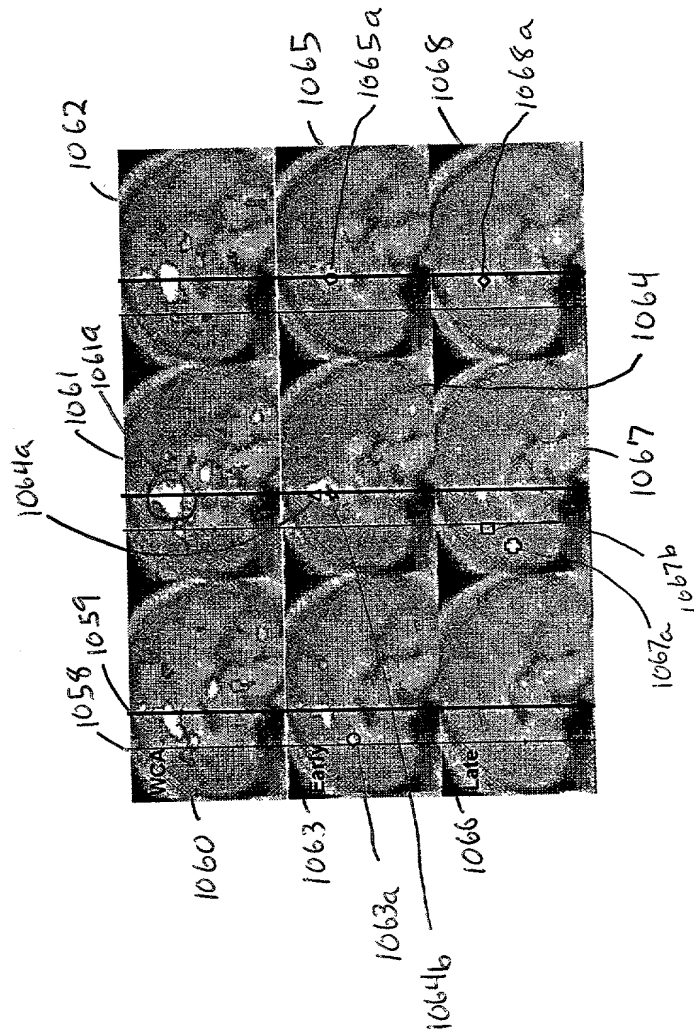
Figure 11E

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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FIG. 11F

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Figure 16

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
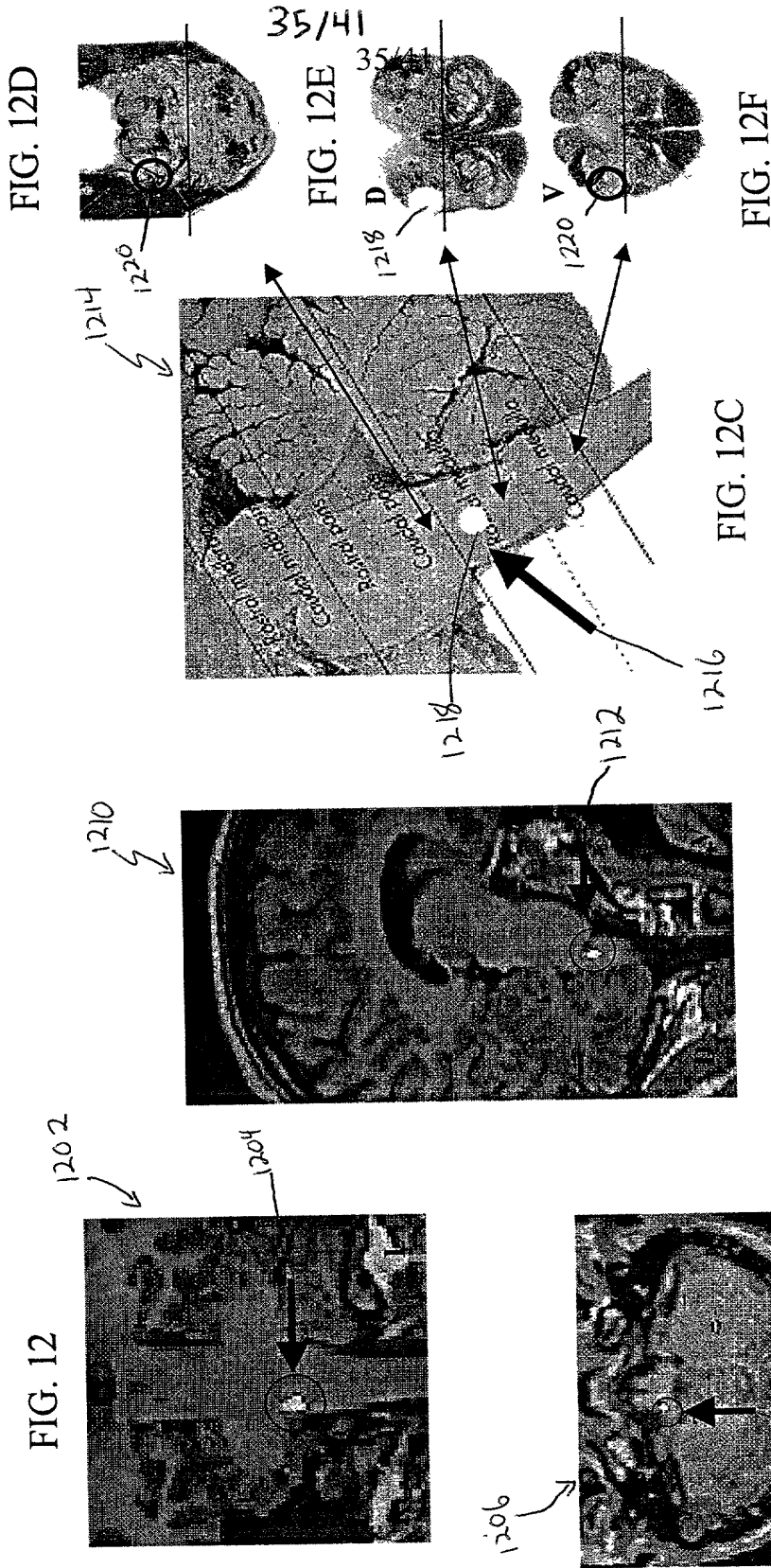Lino Becerra, Et Al.
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Figure 11 H

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Figure 11

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Fig 11J

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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Figure11K

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FIG. 12A

FIG. 12D

FIG. 12E

FIG. 12F

FIG. 12C

FIG. 12B

FIG. 12

FIG. 12A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
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Fig 13

Fig 13A

FIG. 14B

FIG. 14A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
Lino Becerra, Et Al.
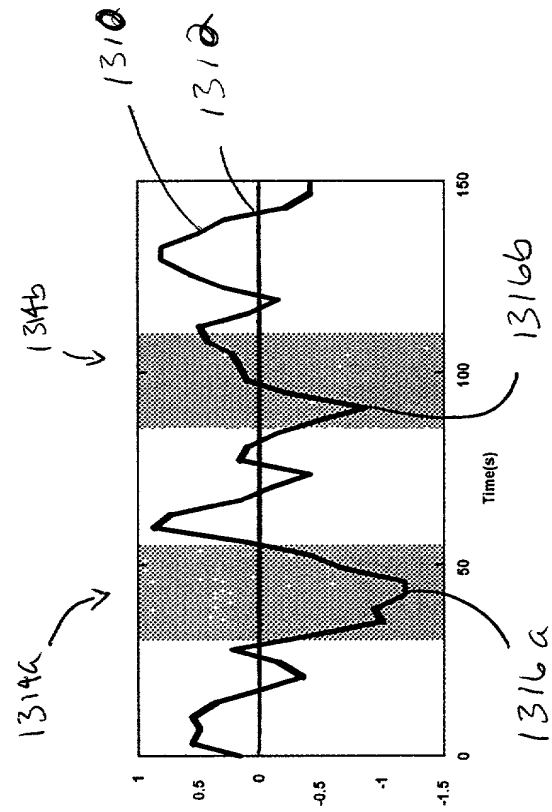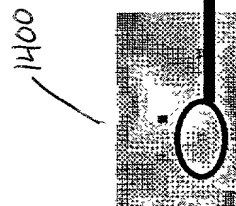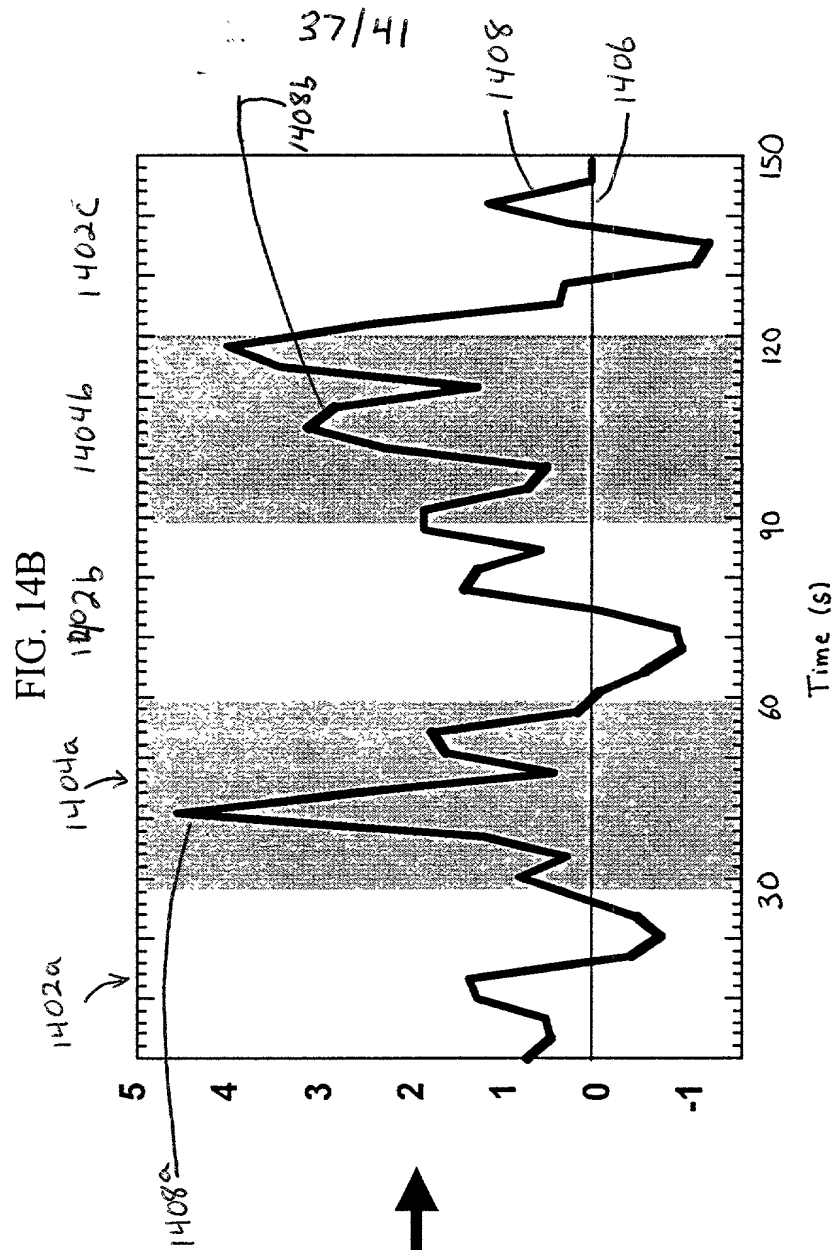CASE NO. MGH-004BUS

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FIG. 15

FIG. 15A

FIG. 15B

FIG. 15C

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
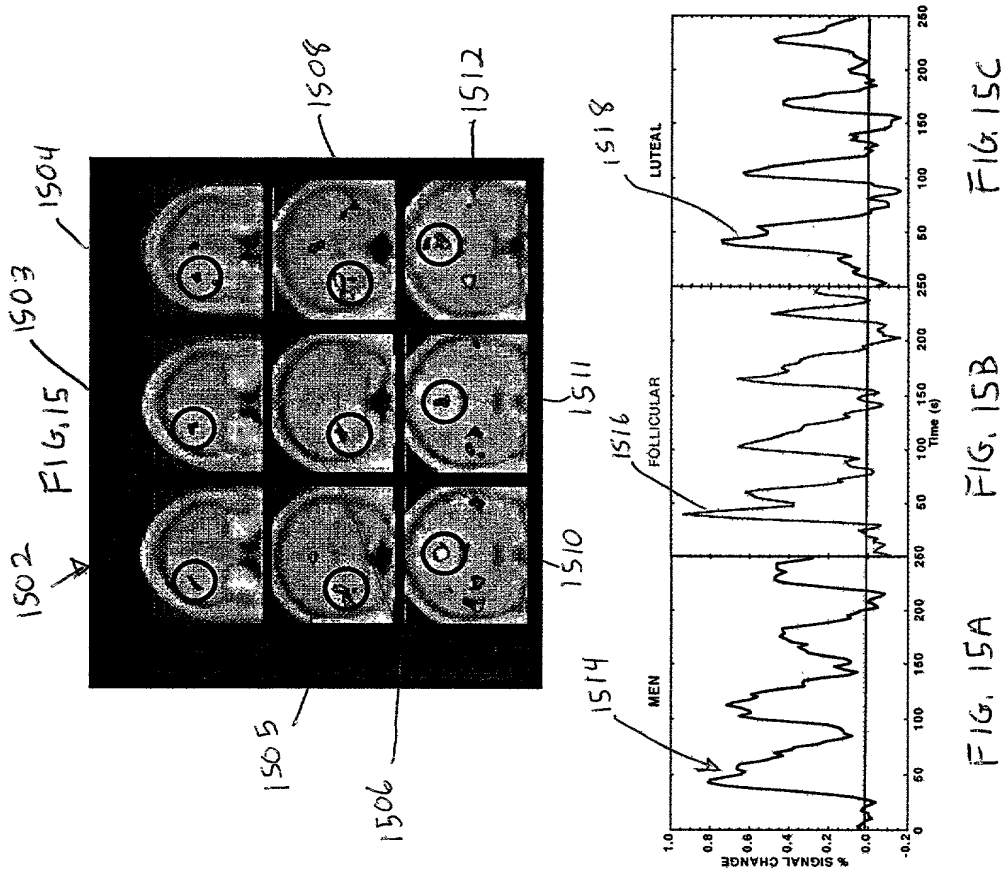Lino Becerra, Et Al.
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Begin

Select Candidates for — 1602
Clinical Testing

Select First and — 1604
Second Subsets of
Candidates

~~Expose Candidate Subsets to~~ — 1606
Administer Drug or Placebo to Candidate Subsets

Perform First — 1608
Neuroimaging Scan

~~Expose Candidate Subsets to~~ 1610   Fig. 16
Administer Drug or Placebo to Candidate Subsets

Perform Second — 1612
Neuroimaging Scan

(A)   ~~Go~~ To Fig. 16 A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
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(B) (from Fig. 16)

Measure physiological and psychophysical Responses of first and second Candidate Subsets — 1614

Measure physiological and psychophysical Responses of First and Second Candidate Subsets — 1616

Correlate Neuroimagging Data with Psychophysical and Physiological Responses — 1618

END

Fig. 16A

METHOD AND APPARATUS FOR OBJECTIVELY MEASURING PAIN,
PAIN TREATMENT AND OTHER RELATED TECHNIQUES
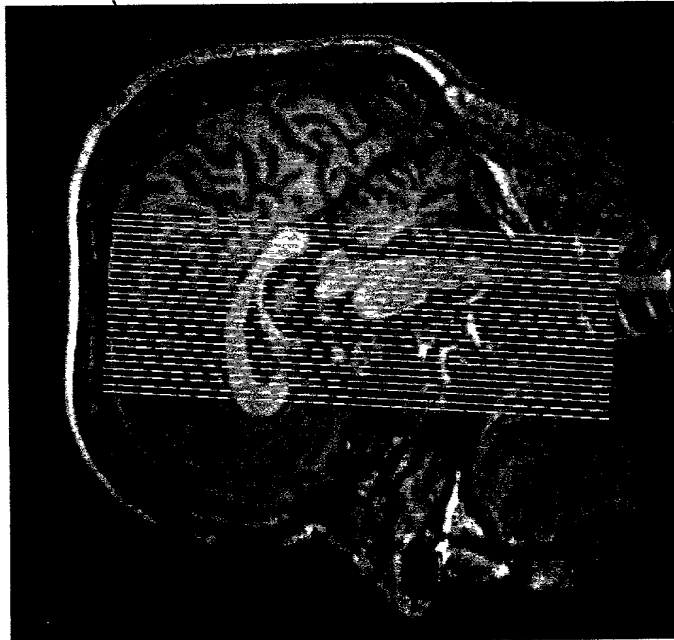Lino Becerra, Et Al.
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Fig. 11

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